IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH,	)
Plaintiff,	)
v.	) Civil Action No.: 06-222 JJF
IMPAX LABORATORIES, INC.,	) **PUBLIC VERSION**
Defendant.	)

DECLARATION OF MARY B. MATTERER
IN SUPPORT OF MOTION FOR PROTECTIVE ORDER TO GOVERN
THE PRODUCTION OF DOCUMENTS IN RESPONSE TO SUBPOENA

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IMPAX LABORATORIES, INC.

Dated: March 20, 2007
Public version filed: March 27, 2007

I, Mary B. Matterer, declare:

1. I am a partner at the law firm of Morris James LLP, counsel to Defendant Impax Laboratories, Inc. ("Impax") in this matter.

2. Attached hereto as Exhibit 1 is a true and correct copy of a Complaint filed on July 26, 2006 in the Eastern District of Texas, C.A. No. 9:06 cv 156-RHC.

3. Attached hereto as Exhibit 2 is a true and correct copy of Alza's Work Plan and Cost Estimate dated May 6, 1992, WYETH 012-000150 - 000164.

4. Attached hereto as Exhibit 3 is a true and correct copy of A Comparative Open-Label, Relative Bioavailability Study of a Microsphere Coated Extended Release Formulation, A Gastrointestinal Therapeutic System (GITS) Formulation, and the Conventional Formulation of Venlafaxine in Healthy Male Volunteers: Final Report, WYETH 022-001711 – 001799.

5. Attached hereto as Exhibit 4 is a true and correct copy of international patent application number PCT/US94/06049.

6. Attached hereto as Exhibit 5 is a true and correct copy of Plaintiff's Responses and Objections to Impax's Third Request for Production of Documents and Things (Nos. 87-124).

7. Attached hereto as Exhibit 6 is a true and correct copy of a November 21, 2006 Alza subpoena.

8. Attached hereto as Exhibit 7 is a true and correct copy of Alza Corporation's Objections and Responses to Subpoena Duces Tecum From Impax Laboratories, Inc.

9. Attached hereto as Exhibit 8 is a true and correct copy of

Stipulated Protective Order Regarding the Production of Documents By Alza Corporation In Response to Subpoena.

10. Attached hereto as Exhibit 9 is a true and correct copy of Defendant's Reply in Support of Motion to Stay Proceedings Pending *Ex Parte* Reexamination of U.S. Patent No. 6,440,457 B1.

11. Attached hereto as Exhibit 10 is a true and correct copy of an email dated February 23, 2007 from Samuel F. Ernst to Wyeth's counsel attaching the stipulated protective order.

12. Attached hereto as Exhibit 11 is a true and correct copy of a letter dated March 5, 2007 from Linda A. Wadler to Samuel F. Ernst.

13. Attached hereto as Exhibit 12 is a true and correct copy of letter dated March 6, 2007 from Samuel F. Ernst to Linda A. Wadler.

14. Attached hereto as Exhibit 13 is a true and correct copy of letter dated March 7, 2007 from Linda A. Wadler to Steven R. Trybus.

15. Attached hereto as Exhibit 14 is a true and correct copy of letter dated March 8, 2007 from Samuel F. Ernst to Linda A. Wadler.

16. Attached hereto as Exhibit 15 is a true and correct copy of letter dated March 12, 2007 from Linda A. Wadler to Samuel F. Ernst.

17. Attached hereto as Exhibit 16 is a true and correct copy of letter dated March 13, 2007 from Samuel F. Ernst to Linda A. Wadler.

18. Attached hereto as Exhibit 17 is a true and correct copy of the Order Granting Defendant's Motion to Stay in *Alza Corporation v. Wyeth and Wyeth Pharmaceuticals, Inc.*, E.D. Texas, CA No. 9:06-CV-156-RHC (Nov. 21, 2006).

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct and that this declaration was executed on this twentieth day of March, 2007 at Wilmington, Delaware.

MARY B. MATTERER (I.D. No. 2696)

EXHIBIT 1

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
LUFKIN DIVISION

ALZA CORPORATION, a Delaware corporation,

Plaintiff,

v.

WYETH, a Delaware corporation, and WYETH PHARMACEUTICALS, INC., a Delaware corporation,

Defendants.

C.A. No. 9:06cv156

JURY TRIAL DEMANDED

COMPLAINT

Plaintiff Alza Corporation ("Alza"), by its undersigned counsel, brings this action for patent infringement against defendants Wyeth and Wyeth Pharmaceuticals, Inc. (collectively "Defendants") and alleges as follows:

Jurisdiction and Venue

1. This action is based upon the Patent Laws of the United States, Title 35 of the United States Code, for infringement of United States Patent No. 6,440,457 ("the '457 Patent").

2. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

3. Venue properly lies in this judicial district under 28 U.S.C. §§ 1391 and 1400(b).

4. This Court has personal jurisdiction over Defendants.

Parties

5. Alza is a Delaware corporation with a principal place of business at 1900 Charleston Road, Mountain View, California 94039.

6. On information and belief, Wyeth is a Delaware corporation with a principal place of business at Five (5) Giraldo Farms, Madison, New Jersey 07940.

7. On information and belief, Wyeth Pharmaceuticals, Inc., is a Delaware corporation with a place of business at 500 Arcola Road, Collegeville, Pennsylvania 19426.

8. On information and belief, Wyeth Pharmaceuticals, Inc., is a subsidiary of Wyeth.

9. On information and belief, at least in part for its own benefit, Wyeth directed, authorized, assisted, cooperated with, or participated in the acts of Wyeth Pharmaceuticals, Inc., about which Alza complains.

Claim of Patent Infringement

10. Alza realleges paragraphs 1 through 9 above as if fully set forth herein.

11. On August 27, 2002, the '457 Patent, entitled "Method of Administering Antidepressant Dosage Form," was duly and legally issued by the United States Patent and Trademark Office to Alza as the assignee of the inventors, David Emil Edgren, Gurdish Kaur Bhatti, Zahedeh Hatamkhani, and Patrick S. L. Wong. The '457 Patent remains in full force and effect and will expire no earlier than August 27, 2019. A true and correct copy of the '457 Patent is attached to this Complaint as Exhibit A.

12. Alza has been and remains the owner of all right, title, and interest in and to the '457 Patent.

13. On information and belief, Defendants contributorily infringe and induce infringement of Claim 1 of the '457 Patent under 35 U.S.C. § 271, including but not limited to

§§ 271(b)-(c) and (f). Defendants contributorily infringe and induce infringement of the '457 Patent through various activities including but not limited to the manufacture, use, sale, and offer for sale of Effexor® XR products in the United States after the '457 Patent issued.

14. On information and belief, Defendants knew of the '457 Patent at all relevant times before making, using, selling, or offering for sale Effexor® XR products.

15. On information and belief, Defendants have in the past offered for sale and sold, and continue to offer for sale and sell Effexor® XR products that constitute a material part of the invention claimed in the '457 Patent and that have no substantial use other than as an infringement of the '457 Patent.

16. On information and belief, Defendants knew and intended that purchasers of Effexor® XR products would use the products in methods so as to infringe the '457 Patent.

17. On information and belief, Defendants have actively induced purchasers of Effexor® XR products to use the products in methods so as to infringe the '457 Patent.

18. On information and belief, purchasers of Effexor® XR products use the products in methods so as to infringe the '457 Patent.

19. On information and belief, Defendants have in the past willfully infringed, and continue to willfully infringe, the '457 Patent through their manufacture, use, sale, and offer for sale of Effexor® XR products.

Prayer For Relief

WHEREFORE, Alza prays for a judgment against Defendants as follows:

(a) adjudging that Defendants have infringed the '457 Patent under 35 U.S.C. § 271;

(b) ordering Defendants to account for and pay to Alza all damages caused to Alza by reason of Defendants' infringement of the '457 Patent, together with prejudgment interest on all damages;

(c) increasing the damages three times based on the willful nature of Defendants' infringement under 35 U.S.C. § 284;

(d) granting Alza its reasonable attorney fees under 35 U.S.C. § 285; and

(e) for such further and additional relief as this Court deems just and proper.

Date: July 26, 2006

By: _____

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Exhibit A

U.S. Patent No. 6,440,457

US006440457B1

(12) **United States Patent**
Edgren et al.

(10) **Patent No.: US 6,440,457 B1**
(45) **Date of Patent: Aug. 27, 2002**

(54) **METHOD OF ADMINISTERING ANTIDEPRESSANT DOSAGE FORM**

(75) Inventors: **David Emil Edgren**, El Granada; **Gurdish Kaur Bhatti**; **Zahedeh Hatamkhani**, both of Fremont; **Patrick S. L. Wong**, Palo Alto, all of CA (US)

(73) Assignee: **Alza Corporation**, Mountain View, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **08/068,480**

(22) Filed: **May 27, 1993**

(51) **Int. Cl.**[7] **A61K 9/22**; A61K 9/52; A61K 31/137; A61P 25/24

(52) **U.S. Cl.** 424/468; 424/457; 424/473; 514/964; 514/654

(58) **Field of Search** 424/473, 468, 424/457; 514/964, 654

(56) **References Cited**

U.S. PATENT DOCUMENTS

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3,133,132	A	5/1964	Loeb et al.	264/49
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3,276,586	A	10/1966	Rosaen	210/90
3,541,005	A	11/1970	Strathmann et al.	210/19
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3,546,142	A	12/1970	Michaels et al.	260/2.1
3,598,122	A	8/1971	Zaffaroni	128/268
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3,845,770	A	11/1974	Theeuwes et al.	128/260
3,916,899	A	11/1975	Theeuwes et al.	128/260
4,063,064	A	12/1977	Saunders et al.	219/121
4,088,864	A	5/1978	Theeuwes et al.	219/121
4,160,020	A	7/1979	Ayer et al.	424/15
4,200,098	A	4/1980	Ayer et al.	128/260
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4,327,725	A	5/1982	Cortese et al.	128/260
4,535,186	A	8/1985	Husbands et al.	564/336
4,611,078	A	9/1986	Husbands et al.	558/410
4,612,008	A	9/1986	Wong et al.	604/892
4,761,501	A	8/1988	Husbands et al.	564/167
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4,842,867	A	6/1989	Ayer et al.	424/473
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Current Therapeutic Research, vol. 42, No. 5, pp. 901–909 (1987) Fabre, Louis F. and Putmanlll, H. Paul An Ascending Single-Dose Tolerance Study of WY-45,030, A Bicyclic Antidepressant in Healthy Men.

J. Am. Phar. Assoc., Sci. Ed., vol. 48, Air-Suspension Technique of Coating Drug Particles, by Wurster Dale E.

J. Am. Pharm. Assoc., vol. 49, pp. 82–84, (1960) Wurster, Dale E., Preparation of Compressed Tablet Granulations by the Air-Suspension Technique II.

Modern Plastics Encyclopedia, vol. 46, pp. 62–70 (1969).

Primary Examiner—Edward J. Webman
(74) *Attorney, Agent, or Firm*—Robert R. Neller

(57) **ABSTRACT**

The invention pertains to a dosage form **10** and to administering an antidepressant medicament **16** for an extended period of time in a rate-known dose.

1 Claim, 1 Drawing Sheet

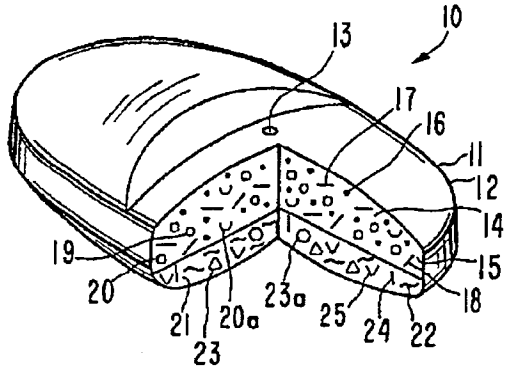


FIG. 1

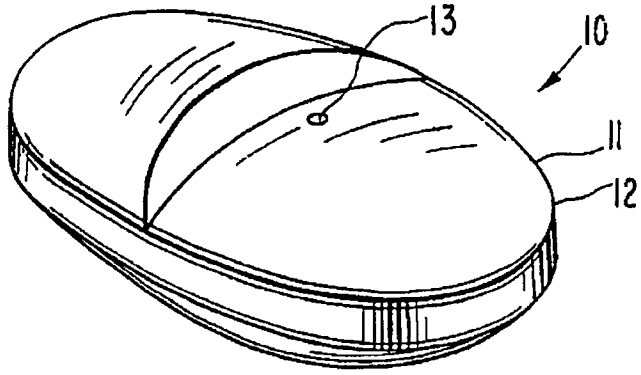


FIG. 2

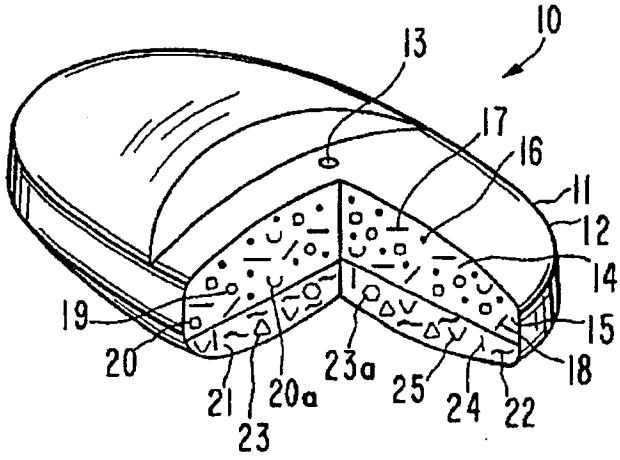
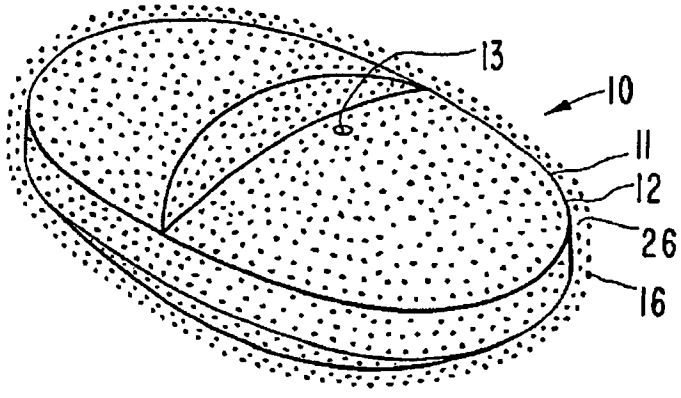


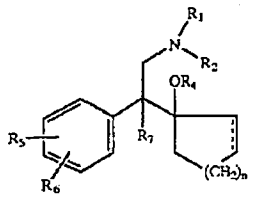
FIG. 3



METHOD OF ADMINISTERING ANTIDEPRESSANT DOSAGE FORM

FIELD OF THE INVENTION

This invention pertains to a controlled-release dosage form comprising a compound of the following structural formula:



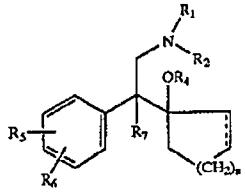
useful for antidepressant therapy. The invention concerns also a method useful for antidepressant therapy by administering the controlled-release dosage form comprising the compound of the formula.

BACKGROUND OF THE INVENTION

The primary goal of drug administration is to provide a therapeutic dose of drug in the body to achieve a desired blood concentration, and then maintain the desired drug blood concentration. The prior art, in attempts to obtain the desired therapeutic effect, often used different dosage forms or programs. One dosage program consists of a single dosing of the drug from a conventional capsule or tablet that produced a rapid rise followed by an immediate decline of the drug blood level versus time. The single dosing does not maintain the drug within a therapeutic range for an extended period of time, but exhibits of a short duration of action due to the inability of the conventional dosage form to provide drug delivery over time.

Another prior art dosing program used to obtain and to achieve drug blood levels consists in administering the drug repetitively using conventional dosage forms at various dosing intervals, as in multiple-dose therapy. In administering a drug according to the multiple-dose therapy, the drug blood level reached and the time required to reach that level depends on the dose and the dosing interval. There are, however, several potential problems inherent in multiple dose therapy. For example, if the dosing interval is not appropriate for the biological half-life of the drug, large peaks and valleys may result in the drug blood levels. Also, the drug blood level may not be within the therapeutic range at sufficiently early times, an important consideration for many disease states. And too, patient noncompliance with the multiple dosing regimen can result in a failure of this approach, especially as a drug in circulation surges to a high each time the drug is administered followed by a decline in drug concentration in the blood and in body compartments. Thus, a graph of drug in circulation following a dosage program of several doses, has an appearance of a series of peaks:, which may surpass the toxic threshold. Then, each time the blood levels decreases into valleys, below a critical level needed to achieve a desired therapeutic effect, that effect may not be obtainable in the blood and body. Conventional dosage forms and their mode of operation are discussed in *Remington's Pharmaceutical Sciences,* 18th Edition, pages 1676 to 1686, (1990), Mack Publishing Co.; *The Pharmacological Basis of Therapeutics,* 7th Edition, page 7 (1985) published by MacMillian Publishing Co., and in U.S. Pat. Nos. 3,598,122 and 3,598,123 both issued to Zaffaroni.

A critical need exists for a controlled-rate dosage form for administering the drug of the formula:



which drug is presently administered in conventional dosage forms including tablets, capsules, elixirs and suspensions. These conventional dosage forms produce the peaks and valleys drug pattern presented above and they do not provide for controlled-rate therapy over an extended period of time. The drug of the formula is dosed twice or thrice a day now because of its elimination half-life of three to five hours. This pattern of dosing indicates the need for a controlled-release dosage form that can administer the drug at a controlled rate over an extended time to provide constant therapy and thereby eliminate the need for multiple dosing. The drugs of the structural formula are known in U.S. Pat. Nos. 4,535,186; 4,611,078; and 4,761,501 all issued to Husbands, Yardley and Muth.

The prior art provided controlled-release dosage forms that can continuously over time administer a drug for controlled-rate therapy. For example, in U.S. Pat. No. 4,327,725 issued to Cortese and Theeuwes and in U.S. Pat. Nos. 4,612,008; 4,765,989; and 4,783,337 issued to Wong, Barclay, Deters, and Theeuwes. The dosage forms disclosed in these patents provide a drug at a constant rate for effecting a therapeutic range for preferred therapy. The dosage forms of the patents provide a therapeutic range and avoids delivering the drug in excess in a toxic range with its accompanying side-effects. The dosage forms of the patents in providing a controlled dose in a therapeutic range also avoids delivering the drug in an ineffective dose in an ineffective range.

The dosage forms presented immediately above operate successfully for their intended use and they can deliver many drugs indicated for good therapy. The drugs of the above structural formula, however, possess properties such as a high solubility of 570 mg per ml at a body temperature of 37° C. that can lead to a premature release of the drug from the dosage form. During operation of the dosage forms, the convection motion of the imbibed fluid, and the hydrostatic pressure of the imbibed fluid coupled with the high solubility can result in the premature release of the drugs of the formula.

It is immediately apparent in the light of the above presentation that an urgent need exists for a dosage form endowed with controlled-release delivery for delivering the drugs embraced by the structural formula. The need exists for the dosage form for delivering the drug at a controlled dose in a therapeutic range while simultaneously providing the intended therapy. It will be appreciated by those versed in the dispensing art, that such a dosage form that can administer the drug in a controlled-rate dose over time, would, represent an advancement and a valuable contribution to the art.

OBJECTS OF THE INVENTION

Accordingly, in view of the above presentation, it is an immediate object of this invention to provide a dosage from

that possesses controlled-release delivery for providing a dosage form for administering a drug of the structural formula.

Another object of the present invention is to provide a dosage form for administering the drug of the formula in a controlled-rate dose in a therapeutic range over a prolonged period of time.

Another object of the present invention is to provide a dosage form that can deliver the drug of the formula essentially-free of a premature release from the dosage form.

Another object of the present invention is to provide a drug delivery controlled-release system that can deliver a drug for maintaining constant drug levels in the blood thereby functioning as a prolonged release system.

Another object of the present invention is to provide drug delivery sustained-release system that provides slow release of the drug over an extended period of time optionally in a therapeutic range.

Another object of the present invention is to provide a dosage form that substantially reduces and/or substantially eliminates the unwanted influences of a gastrointestinal environment of use and still provides controlled drug administration.

Another object of the present invention is to provide an improvement in a dosage form for administering a drug embraced by the structural formula and its pharmaceutically acceptable salt, wherein the improvement comprises delivering the drug in a controlled-release rate from the dosage form for improved and known therapy.

Another object of the invention is to provide a once-a-day controlled-release dosage form to deliver the drug of the structural formula orally to a patent in need of therapy.

Another object of the invention is to provide a method for administering a drug of the formula by orally administering the drug in a controlled rate dose per unit dose over an extended time to an animal in need of therapy.

Another object of the present invention is to provide a method for administering a drug of the formula in a therapeutic range while simultaneously substantially-avoiding a toxic range and an infective range.

Another object of the present invention is to provide a therapeutic composition comprising a drug of the structural formula blended with a drug-composition forming polymer.

Another object of the invention is to provide a therapeutic composition comprising a member selected from the group consisting of venlafaxine and its pharmaceutically acceptable additional salt and a pharmaceutically acceptable polymer carrier for venlafaxine and its acceptable salts.

Other objects, feature, and advantages of the invention will more apparent to those versed in the dispensing arts from the following detailed specification, taken in conjunction with the drawings and the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawing figures, which are not drawn to scale, but are set forth to illustrate various embodiments of the invention, the drawing figures are as follows:

Drawing FIG. 1 is a general view of a dosage form provided by the invention, which dosage form is designed and shaped for oral administration, and for a drug delivery in a controlled-rate dose in the gastrointestinal tract;

Drawing FIG. 2 is an opened view of the dosage form of drawing FIG. 1 for depicting the structure of the dosage form and the composition member contained inside the dosage form; and

Drawing FIG. 3 is a view of a dosage form that depicts an external, instant-release of drug of the structural formula coated on the exterior surface of the dosage form.

In the drawing figures, and in the specification, like parts in related figures are identified by like numbers. The terms appearing earlier in the specification and in the description of the drawing figures, as well as embodiments thereof, are further described elsewhere in the disclosure.

DETAILED DESCRIPTION OF THE DRAWINGS

Turning now to the drawing figures in detail, which drawing figures are examples of dosage forms provided by this invention, and which examples are not to be construed as limiting, one example of a dosage form is seen in drawing FIG. 1. In drawing FIG. 1, a dosage form **10** is seen comprising a body member **11**, which body 11 comprises wall **12**, that surrounds and forms an internal area, not seen in drawing FIG. 1. Dosage form **10** comprises at least one exit port **13** for connecting the exterior with the interior of dosage form **10**.

The dosage form **10** of drawing FIG. 1 illustrates a controlled-release dosage form manufactured as an osmotic dosage form that delivers a drug by osmotic action over an extended period of time. The dosage form comprising controlled-release properties embraced by this invention are successful at maintaining substantially constant drug levels in the blood or in a tissue. The dosage forms within the mode and manner of this invention comprises also sustained-release dosage forms. The sustained-release dosage forms releases the drug and provide drug levels in the blood or target tissue within a therapeutic range over an extended period of time. The invention embraces additionally prolonged release dosage forms. The prolonged release dosage form denotes extended duration of drug delivery action over that achieved by conventional drug delivery.

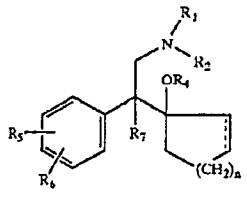
In drawing FIG. 2, dosage form **10** of FIG. 1 is seen in opened section. In drawing FIG. 2, dosage form **10** comprises a body **11**, a wall **12** that surrounds and defines an internal compartment **14**. In drawing FIG. 2, internal compartment **14** communicates through an exit passageway **13** with the exterior of dosage form **10**.

Wall **12** of dosage form **10** comprises totally or in at least a part of a composition that is permeable to the passage of an exterior fluid present in an environment of use, such as aqueous and biological fluids. Wall **12** is formed of nontoxic ingredients, is substantially impermeable to the passage of a drug and other ingredients present in compartment **14**. Wall **12** comprises a composition that is substantially inert, that is, wall **12** maintains its physical and chemical integrity during the drug dispensing life of a drug from dosage form **10**. The phrase, "maintaining its physical and chemical integrity," means wall **12** does not lose its structure and it does not change during the dispensing life of dosage form **10**, except for possible leaching of one or more exit **13** passageway formed during operation of dosage form **10** or for leaching a water-soluble flux enhancers blended into wall **12**. Wall **12** comprises a material that does not adversely affect an animal, a human or any other components comprising the dosage form. Representative materials for forming wall **12**, are in one embodiment, a cellulose ester polymer, a cellulose ether polymer and a cellulose esterether polymer. These cellulosic polymers have a degree of substitution. D.S., on the anhydroglucose unit, from greater than 0 up to 3 inclusive. By degree of substitution is meant the average number of hydroxyl groups originally present on the anhydroglucose unit comprising the cellulose polymer that are replaced by a

substituting group. Representative materials include a member selected from the group consisting of cellulose acylate, cellulose diacylate, cellulose triacylate, cellulose acetate, cellulose diacetate, cellulose triacetate, mono-, di- and tricellulose alkanylates, mono-, di-, and tricellulose aroylates, and the like. Exemplary polymers include cellulose acetate having a D.S. up to 1 and an acetyl content up to 21%; cellulose acetate having a D.S. of 1 to 2 and an acetyl content of 21 to 35 %; cellulose acetate having a D.S. of 2 to 3 and an acetyl content of 35 to 44.8%, and the like. More specific cellulosic polymers include cellulose propionate having a D.S. of 1.8 and a propyl content of 39.2 to 45% and a hydroxyl content of 2.8 to 5.4%; cellulose acetate butyrate having a D.S. of 1.8, an acetyl content of 13 to 15% and a butyryl content of 34 to 39%; cellulose acetate butyrate having an acetyl content of 2 to 29%, a butyryl content of 17 to 53% and a hydroxyl content of 0.5 to 4.7; cellulose triacylates having a D.S. of 2.9 to 3 such as cellulose trivalerate, cellulose trilaurate, cellulose tripolmitate, cellulose trisuccinate, and cellulose trioctanoate; cellulose diacylates having a D.S. of 2.2 to 2.6 such as cellulose disuccinate, cellulose dipalmitate, cellulose dioctanoate, cellulose dipentanoate, co-esters of cellulose such as cellulose acetate butyrate and cellulose acetate propionate, and the like.

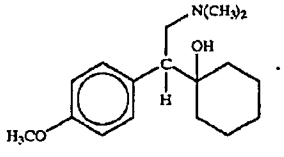
Additional polymers include ethyl cellulose of various degree of etherification with ethoxy content of from 40% to 55%, acetaldehyde dimethyl cellulose acetate, cellulose acetate ethyl carbamate, cellulose acetate methyl carbamate, cellulose acetate diethyl aminoacetate, semipermeable polyamides; semipermeable polyurethanes; semipermeable sulfonated polystyrenes; semipermeable cross-linked selective polymers formed by the coprecipitation of a polyanion and a polycation as disclosed in U.S. Pat Nos. 3,173,876, 3,276,586, 3,541,005; 3,541,006, and 3,546,142; semipermeable polymers as disclosed by Loeb and Sourirajan in U.S. Pat. No. 3,133,132; semipermeable lightly cross-linked polystyrene derivatives, semipermeable cross-linked poly (sodium styrene sulfonate); semipermeable cross-linked poly(vinylbenzyltrimethyl ammonium chloride); semipermeable polymers exhibiting a fluid permeability of 2.5×10^{-8} to 2.5×10^{-4} (cm^2/hr.atm) expressed per atmosphere of hydrostatic or osmotic pressure difference across the semipermeable wall. The polymers are known to the art in U.S. Pat. Nos. 3,845,770; 3,916,899; and 4,160,020; and in *Handbook of Common Polymers* by Scott, J. R. and Roff, W. J., 1971 published by CRC Press, Cleveland, Ohio.

Compartment **14** comprises a drug composition, identified as drug layer **15** which contains drug **16**, identified by dots. Drug **16** comprises a drug of the following structural formula:



wherein the dotted line represents optional unsaturation or a cycloalkenyl moiety; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl, an alkyd of 1 to 6 carbon atoms, an alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms in which each alkyl group comprises 1 to 6 carbon atoms, alkanamido of 2 to 7 carbon atoms, halo, and trifluoroethyl, R_7 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbons, and n is one of the integers 0, 1, 2, 3, and 4. The formula embraces also the pharmaceutically acceptable addition salts including a member selected from the group consisting of inorganic, organic, hydrochloric, hydrobromic, gluconic, fumaric, maleric, sulfonic, succinic, sulfuric, phosphoric, tartaric, acetic, proponic, citric, oxalic and similar pharmaceutically acceptable addition salts. The compounds are known in U.S. Pat. Nos. 4,535,186; 4,611,078; 4,761,501; and 5,190,765.

The drugs of the structural formula are represented by the drug 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl] cyclohexanol of the structural formula:



The drug embraced by the formula possesses antidepressant properties. The drug in vitro prevents the neuronal uptake of serotonin, morepinephrine, and dopamine and it does not inhibit monoamine oxidase. The drug antagonizes reserpine-induced hypothermia and potentiates the effects of levodopa, and reduces histamine-induced corticotropin release and induces cyclicadenosine monophosphate subsensitivity after both acute and chronic administration. The drug possesses excellent antidepressant activity in humans. The therapeutic amount of drug **16** in dosage form **10** is 0.5 mg to 750 mg, with individual dosage forms comprising 2, 5, 10, 25, 40, 50, 75, 100, 150, 250, 300, 500, and 600 mg of drug **16** for administering in a single dose or in more then one dose over an extended period of 24 hours. The therapeutic properties of the drug embraced by the structural formula are reported in *Current Therapeutic Research*, Vol. 42, No. 5, pages 901 to 909 (1987).

Composition **15** comprising drug **16** may comprise a drug dispensing carrier and composition formulating member consisting of a member selected from the group consisting of 0 wt % to 25 wt % of a hydroxypropylalkylcellulose where alkyl consists of 1 to 7 carbons selected from the group consisting of methyl, ethyl, isopropyl, butyl, pentyl, and hexyl which cellulose member comprises a 9,000 to 1,250,000 molecular weight and is exemplified by hydroxypropylmethylcelluose, hydroxypropylethylcellulose, hydroxypropylisopropylcellulose, hydroxypropylbutylcellulose and hydroxypropylhexylcellulose represented by dashes **17**; a member selected from the group consisting of 0 wt % to 20 wt % hydroxylalkylcellulose where alkyl is 1 to 6 carbons including methyl, ethyl, propyl, butyl, pentyl, and hexyl which cellulose member comprises a 7,500 to 750,000 molecular weight and is exemplified by hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyisopropylcellulose and

hydroxybutylcellulose as represented by slanted line 18; a member selected from the group consisting of 0 wt % to 35 wt % of a vinyl-polymer having a 3,500 to 750,000 molecular weight represented by poly-n-vinylamide, poly-n-vinlycetamide, poly-n-vinylethylacetamide, poly-n-vinylmethylpropionamide, poly-n-vinyl ethylpropionamide, poly-n-vinylmethylisobutyramide, poly-n-vinyl-2-pyrrolidone, poly-n-vinypiperidone also known as polyvinylpyrrolidone and as poly-n-vinylpyrroledone, poly-n-vinylcaprolactam, poly-n-vinyl-5-methyl-2-pyrrolidone and poly-n-vinyl-3-methyl-2-pyrrolidone, and poly-n-vinylpyrrolidone copolymer with a member selected from the group consisting of vinyl acetate, vinyl alcohol, vinyl chloride, vinyl fluoride, vinyl butyrate, vinyl laurate and vinyl stearate represented by small circles **19**; and 0 wt %, where wt % is weight percent, 35 wt % of a maltodextrin polymer composition comprising the formula $(C_6H_{12}O_5)_n H_2O$ wherein n is 3 to 7,500 and the maltodextrin polymer comprises a 500 to 1,250,000 number average molecular weight represented by a small square **20**; as member selected from the group consisting of 0 wt % to 40 wt % of poly(etheylen oxide) having a molecular weight of 100,000 to 600,000 grams per mole, represented by half-circles **20***a*. Composition **15** optionally comprises from 0 to 4.5 wt % of a lubricant represented by magnesium stearate, calcium stearate or stearic acid. The total weight of all ingredients in composition **15** is equal to 100 wt %, weight percent.

Compartment **14** comprises a displacement composition or push layer **21**. Displacement composition **21** comprises a polymer member selected from the group consisting of a polymer possessing a repeating molecular unit $-(O-CH_2CH_2)_n-$ wherein n is a positive whole number of 50,000 to 300,000 as represented by a poly(alkylene oxide) comprising poly(ethylene oxide) seen as wavy line **22**; a maltodextrin polymer of the formula $(C_6H_{12}O_5)_n H_2O$ wherein n is 50 to 62,000 and comprises a 9,000 to 10,000,000 molecular weight and represented by triangle **23**; a carboxymethylcellulose polymer comprising a 10,000 to 5,000,000 molecular weight represented by alkali carboxymethylcellulose, sodium carboxymethylcellulose and potassium carboxymethylcellulose, ammonium carboxymethylcellulose, sodium carboxymethyl-2-hydroxyethylcellulose, sodium carboxymethylmethylcellulose, alkali carboxymethyl-hydroxypropylmethylcellulose, alkali carboxymethyl-2-hydroxyethylmethylcellulose, alkali carboxymethyl-2-hydroxybutylmethylcellulose, alkali carboxymethyl-2-hydroxyethyl-ethylcellulose and alkali carboxymethyl-2-hydroxypropylcellulose, where alkali is sodium and potassium and seen in drawing FIG. 2 as hexagonal **23***a*. The polymers in push layer **21** provide unfureseen operating advantages as the polymer maintains its chemical composition during operation as it imbibes an external aqueous fluid including biological fluid while simultaneously pushing the drug from the dosage form essentially-free of substantially mixing the drug composition with the push composition. The displacement composition **21** comprises optionally from 4 to 35 wt % of an osmotically active compound, also known as osmagent and represented by vertical line **24**. Representative of osmotically effective compounds comprises salts, oxides, esters that exhibit imbibition properties, carbohydrates and acids including a member selected from the group consisting of magnesium sulfate, magnesium chloride, sodium chloride, lithium chloride, potassium chloride, potassium sulfate, sodium sulfate, sodium sulfite, lithium sulfate, ammonium chloride, potassium lactate, mannitol, urea,: magnesium succinate, tartaric acid, raffinose, sorbitol, sucrose, fructose, and glucose. Displacement layer **21** optionally comprises 0.5 wt % to 30 wt % of a cellulose polymer **25** represented by the letter v. Representative of cellulose polymer **25** comprise a member selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxypropylethylcellulose, hydroxypropylisopropylcellulose, hydroxypropylbutylcellulose, hydroxypropylpentylcellulose, and hydroxypropylhexylcellulose comprising a 9,000 to 225,000 molecular weight. The displacement composition optionally comprises 0 wt % to 5 wt % of lubricant stearic acid and, magnesium stearate, calcium oleate, oleic acid, and caprylic acid. The polymers are known in U.S. Pat Nos. 3,845,770; and 4,160,020; in *Handbook of Common Polymers* by Scott, J. R., and Roff, W. J., published by CRC Press, Cleveland, Ohio.

Dosage form **10**, a seen in drawing FIG. **3** depicts another preferred manufacture provided by the invention. Dosage form **10**, in drawing FIG. **3**, comprises an external coat on a the exterior surface of dosage form **10**. Coat **26** is a therapeutic composition comprising 10 mg to 150 mg of drug **16**, represented by dots **16**. Exterior coat **26** provides instant drug **16** for instant therapy. Drug **16** is blended with an aqueous-soluble composition comprising a carrier methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and blends of hydroxypropylcellulose and hydroxypropylmethylcellulose. Coat **26** optionally comprises polyethylene glycol or acetylated triglycerides. Coat **26** provides instant therapy as coat **26** dissolves or undergoes dissolution in the presence of a biological fluid and concurrently therewith delivers drug **16** to a drug receiving patient. Coat **26** provides instant therapy and it essentially overcomes the time required for the drug to be delivered from the dosage form.

Dosage form **10**, as provided by this invention, and as seen in the above drawing figures can be manufactured for administering drug **16** by the oral route, and in another embodiment, dosage form **10** comprising exterior and interior drug **16** can be sized and shaped for administering drug **16** by the sublingual and buccal routes. The sublingual and buccal routes can be used for quicker therapy and they can be used when a smaller dose of drug **16** is needed for therapy. The buccal and sublingual routes can be used as a by-pass of the first pass of hepatic metabolism of drug **16**. The sublingual or buccal routes can be used for administering the first dose of drug, followed by permitting dosage form **10** to enter the gastrointestinal tract for subsequent drug delivery.

Dosage form **10**, when manufactured as an osmotic, controlled-release dosage form, comprises at least one passageway **13**, or more than one passageway **13**. The expression "at least one passageway" includes aperture, orifice, bore, pore, porous element through which the drug can be pumped, diffuse, travel or migrate, hollow fiber, capillary tube, porous overlay, porous insert, microporous member, porous composition, and the like. The expression also includes a material that erodes or is leached from wall **12** in the fluid environment of use to produce at least one passageway in dosage form **10**. Representative material suitable for forming at least one passageway, or a multiplicity of passageways, includes an erodible poly(glycolic) acid or poly(lactic) acid member in the wall; a gelatinous filament; poly(vinyl alcohol); leachable materials such as fluid removable pore forming polysaccharides, salts, or oxides, and the like. A passageway or a plurality of passageways can be formed by leaching a material such as sorbitol, sucrose,

lactose, fructose, or the like, from the wall to provide an osmotic dimensioned pore-passageway. The passageway can have any shape such as round, triangular, square, elliptical, and the like, for assisting in the metered release of drug from dosage form **10**. Dosage form **10** can be constructed with one or passageways in spaced apart relation on one or more than a single surface of a dosage form. Passageways and equipment for forming passages are disclosed in U.S. Pat. Nos. 3,845,770 and 3,916,899 by Theeuwes and Higuchi; in U.S. Pat No. 4,063,064 by Saunders et al; and in U.S. Pat. No. 4,088,864 by Theeuwes et al. Osmotic passageways comprising controlled-drug releasing dimension, sized, shaped and adapted as a drug releasing pore formed by aqueous leaching to provide a drug-releasing pore of controlled osmotic release rate are disclosed in U.S. Pat. No. 4,200,098 by Ayer and Theeuwes; and in U.S. Pat. No. 4,285,987 by Ayer and Theeuwes.

Wall **12** of osmotic dosage form **10** can be formed in one technique using the air suspension procedure. This procedure consists in suspending and tumbling the compressed drug-push core laminate in a current of air and wall forming composition until a wall is applied to the drug-push compartment. The air suspension procedure is well-suited for independently forming the wall. The air suspension procedure is described in U.S. Pat. No. 2,799,241; *J. Am. Pharm. Assoc.*, Volume 48, pages 451 to 454, (1959); and ibid, Volume 49, pages 82 to 84, (196). Osmotic dosage forms can also be coated with a wall forming composition in a Wurster® air suspension coater, using methylene dichloride-methanol cosolvent, 80:20, wt:wt, an ethanol-water, or acetone-water cosolvent, 95:5 wt:wt using 2.5 to 4% solids. The Aeromatic® air suspension coater using a methylene dichloride-methanol cosolvent, 80:20 wt:wt, also can be used for applying the wall. Other wall forming techniques such as pan coating system, where wall forming compositions are deposited by successive spraying of the composition on the drug-push compartment, accompanied by tumbling in a rotating pan. Finally, the wall coated compartments are dried in a forced air over at 30° C. to 50° C. for up to a week to free dosage form **10** of solvent. Generally, the walls formed by these techniques have a thickness of 2 to 30 mils with a presently preferred thickness of 4 to 10 mils.

Dosage form **10** of the invention is manufactured by standard manufacturing techniques. For example, in one manufacture the beneficial drug and other ingredients comprising the drug layer facing the exit means are blended and pressed into a solid layer. The drug and other ingredients can be blended with a solvent and mixed into a solid or semisolid formed by conventional methods such a ball-milling, calendering, stirring or rollmilling and then pressed into a preselected shape. The layer possesses dimensions that correspond to the internal dimensions of the area the layer is to occupy in the dosage form and it also possesses dimensions corresponding to the second layer for forming a contacting arrangement therewith. Next, the push layer, is placed in contact with the drug layer. The push layer is manufactured using techniques for providing the drug layer. The layering of the drug layer and the push layer can be fabricated by conventional press-layering techniques. Finally, the two layer compartment forming members are surrounded and coated with an outer wall. A passageway is laser, leached, or mechanically drilled through the wall to contact the drug layer, with the dosage form optically oriented automatically by the laser equipment for forming the passageway on the preselected surface when a laser is used for forming the passageway.

In another manufacture, the dosage form is manufactured by the wet granulation technique. In the wet granulation technique, for example, the drug and the ingredients comprising the drug layer are blended using an organic solvent, such as isopropyl alcohol-ethylene dichloride 80:20 v:v (volume:volume) as the granulation fluid. Other granulating fluid such as denatured alcohol 100% can be used for this purpose. The ingredients forming the drug layer are individually passed through a 40 mesh screen and then thoroughly blended in a mixer. Next, other ingredients comprising the drug layer are dissolved in a portion of the granulation fluid, such as the cosolvent described above. Then the latter prepared wet blend is slowly added to the drug blend with continual mixing in the blender. The granulating fluid is added until a wet blend is produced, which wet mass then is forced through a 20 mesh screen onto oven trays. The blend is dried for 18 to 24 hours at 30° C. to 50° C. The dry granules are sized then with a 20 mesh screen. Next, a lubricant is passed through an 80 mesh screen and added to the dry screen granule blend. The granulation is put into milling jars and mixed on a jar mill for 1 to 15 minutes. The push layer is made by the same wet granulation techniques. The compositions are pressed into their individual layers in a Manesty® press-layer press.

Another manufacturing process that can be used for providing the compartment-forming composition layers comprises blending the powered ingredients for each layer independently in a fluid bed granulator. After the powered ingredients are dry blended in the granulator, a granulating fluid, for example, poly(vinyl-pyrrolidone) in water, or in denatured alcohol, or in 95:5 ethyl alcohol/water, or in blends of ethanol and water is sprayed onto the powders. Optionally, the ingredients can be dissolved or suspended in the granulating fluid. The coated powders are then dried in a granulator. This process granulates all the ingredients present therein while adding the granulating fluid. After the granules are dried, a lubricant such as stearic acid or magnesium stearate is added to the granulator. The granules for each separate layer are pressed then in the manner described above.

The dosage form of the invention is manufactured in another manufacture by mixing a drug with composition forming ingredients and pressing the composition into a solid lamina possessing dimensions that correspond to the internal dimensions of the compartment. In another manufacture the drug and other drug composition-forming ingredients and a solvent are mixed into a solid, or a semisolid, by conventional methods such as ballmilling, calendering, stirring or rollmilling, and then pressed into a preselected layer forming shape. Next, a layer of a composition comprising an osmopolymer and an optional osmagent are placed in contact with the layer comprising the drug. The layering of the first layer comprising the drug and the second layer comprising the osmopolymer and optional osmagent composition can be accomplished by using a conventional layer press technique. The wall can be applied by molding, spraying or dipping the pressed bilayer's shapes into wall forming materials. Another and presently preferred technique that can be used for applying the wall is the air suspension coating procedure. The procedure consists in suspending and tumbling the two layers in current of air until the wall forming composition surrounds the layers. The air suspension procedure is described in U.S. Pat. No. 2,799,241; *J. Am. Pharm. Assoc.*, Vol. 48 pp 451–454 (1979); and, ibid, Vol. 49, pp 82–84 (1960). Other standard manufacturing procedures are described in *Modern Plastics Encyclopedia*, Vol 46, pp 62–70 (1969); and in *Pharmaceu-*

tical Science, by Remington, 14th Ed., pp 1626–1678 (1970), published by Mack Publishing Co., Easton, Pa.

Exemplary solvents suitable for manufacturing the wall, the laminates and laminae include inert inorganic and organic solvents final laminated wall. The solvents broadly include members selected for the group consisting of aqueous solvents, alcohols, ketones, esters, ethers, aliphatic hydrocarbons, halogenated solvents, cyclaliphatics, aromatics, heterocyclic solvents and mixtures thereof. Typical solvents include acetone, diacetone, alcohol, methanol, ethanol, isopropyl alcohol, butyl alcohol, methyl acetate, ethyl acetate, isopropyl acetate, n-butyl acetate, methyl isobutyl ketone, methyl propyl ketone, n-hexane, n-heptaene ethylene glycol monoethyl ether, ethylene glycol monoethyl acetate, methylene dichloride, ethylene dichloride, propylene dichloride, carbon tetrachloride, chloroform, nitroethane, nitropropane, tetrachoroethan, ethyl ether, isopropyl ether, cyclohexane, cyclooctane, benzene, toluene, naphtha, tetrahydrofuran, diglyme, aqueous and nonaqueous mixtures thereof, such as acetone and water, acetone and methanol, acetone and ethyl alcohol, methylene dichloride and methanol, and ethylene dichloride and methanol.

DETAILED DISCLOSURE OF EXAMPLES OF THE INVENTION

The following examples are merely illustrative of the present invention and they should not be considered as limiting the scope of the invention in any way as these examples and other equivalents thereof will become apparent to those versed in the art in the light of the present disclosure, the drawings and accompanying claims.

Example 1

A dosage form adapted for delivering a drug in a therapeutic range is manufactured as follows: first a displacement or push layer is prepared by blending and passing through a stainless steel sizing screen having a mesh opening of 420 microns 587.5 grams of sodium carboxymethylcellulose having a degree of polymerization of approximately 3,200 and a degree of substitution of 0.7 carboxymethyl groups per anhydroglucose unit, 300 grams of powdered sodium chloride, 50 grams of hydroxypropylcellulose having a molecular weight of approximately 60,000 grams per mole, and 50 grams of hydroxypropylmethylcellulose having an average methoxyl content of 29 weight percent and an average hydroxypropyl content of 10 weight percent and an average molecular weight of approximately 11,300 grams per mole. Next 10 grams of red ferric oxide were passed through a sizing screen having openings of approximately 250 microns. The resulting powders were mixed in a planetary mixer to a uniform blend. The resulting blend was wet granulated by adding with stirring anhydrous ethyl alcohol until, a cohesive mass was formed. This mass was passed through a sizing screen having openings of approximately 840 microns, forming coated displacement particles, which were an dried overnight at ambient temperature and humidity. The dried particles were then passed again through the 840 micron sizing screen. Next 2.5 grams of magnesium stearate, which had been previously sized through a mesh having 180 micron openings, were tumble mixed into the coated particles.

A composition comprising a drug of the structural formula was prepared as follows: first, a drug composition was prepared by passing 840 grams of venlafaxine hydrochloride, 100 grams of hydroxypropylcellulose having a molecular weight of approximately 60,000 grams per mole, and 50 grams of polyvinylpyrrolidone having a molecular weight of approximately 40,000 grams per mole, were passed through a sizing having openings of approximately 420 microns, and mixed in a planetary mixer to yield a uniform blend. Then, anhydrous ethyl alcohol was added to the mixture with stirring to produce a cohesive damp mass. The resulting damp mass was sized through a sieve having an opening of 840 microns, producing coated venlafaxine drug, which was air dried overnight. The resulting dried coated venlafaxine drug was passed again through the sizing screen having an 840 micron opening. Next, 10 grams of magnesium stearate, sized to 180 microns, was tumble mixed into the blend.

Next, the displacement-push composition and the drug composition were formed into a bilayer core as follows: first, 87 mg of the drug composition was placed in a 9/32 inch round die cavity and lightly tamped with a standard concave round tooling to form a slightly cohesive layer. Then, 70 mg of push composition was added to die and the and the resulting fill was compressed with a final force of 2 tons, thereby forming a two layer cores.

The bilayer cores were placed next in a coating pan having a 12 inch diameter and they were coated with a wall-forming solution. The wall-forming solution was prepared by dissolving 380 grams of cellulose acetate having an acetyl content of 39.8 weight percent in 7,220 grams of acetone. In a separate mixing vessel, 20 grams of polyethylene glycol having a molecular weight of approximately 3,350 grams per mole were dissolved in approximately 380 grams of purified water. The two solutions were mixed to form the wall-coating solution which was spray coated onto the cores until about 20 mg of wall composition was deposited on the surfaces of the bilayer core.

A delivery exit port was formed across the wall by drilling an exit port, centered on the face of the dosage form on the drug composition side of the dosage form. The resulting dosage form was placed in simulated physiological fluid at 37° C., and the dosage form delivered a dose of 73 mg of venlafaxine hydrochloride at a controlled, zero rate over an extended duration of 15 hours.

Example 2

The procedure of Example 1 was followed with the manufacturing procedures as set forth, except that the drug composition comprises 890 grams of venlafaxine hydrochloride, 100 grams of hydroxypropylcellulose, and 10 grams of magnesium stearate. The resulting dosage form released in simulated intestinal fluid 77 mg of venlafaxine hydrochloride at a zero-order rate over an extended duration of 16 hours.

Example 3

The procedure of Example 1 was followed with all manufacturing steps as described, except that the drug composition consists of 650.0 grams of venlafaxine hydrochloride, 240.0 grams of maltodextrin having an average molecular weight of approximately 1800 grams per mole and an average degree of polymerization of 11.1, 80.0 grams of hydroxypropyl cellulose, 20.0 grams of polyvinyl pyrrolidone, and 10.0 grams of magnesium stearate. The resulting dosage form was tested in artificial intestinal fluid, the dosage form delivered a dose of 57 mg of venlafaxine hydrochloride at zero order rate over a period of 15 hours.

Example 4

The procedure of Example 1 was repeated with the manufacture as previously set-forth, except that the drug

composition consists of 840.0 grams of venlafaxine hydrochloride, 150.0 grams of polyethylene oxide having an average molecular weight of approximately 100,000 grams per mole, and 10.0 grams of magnesium stearate. The wall weight weighed approximately 25 mg. The resulting dosage forms were tested in simulated intestinal fluid, and they released a dose of 73 mg of venlafaxine hydrochloride at controlled rate over an extended period of 20 hours.

Example 5

The compositions were manufactured as in Example 1. The process of manufacture was the same except that the push layer manufactured was prepared in a fluid bed aqueous-based granulation process. This was accomplished by sizing the sodium carboxymethyl cellulose, the sodium chloride, the hydroxypropyl cellulose, and red ferric oxide through a screen having openings of 420 microns. The resulting powders were charged into a fluid bed granulation column and binder solution consisting of the hydroxypropyl methylcellulose at a 5 percent solids concentration in water was sprayed on, thereby forming the granules for the push layer.

Example 6

The compositions and processes followed in this example were the same as in Example 1 except the push consisted of 740.0 grams polyethylene oxide with an average molecular weight of approximately 5 million grams per mole, 200.0 grams of sodium chloride, 50.0 grams of hydroxypropyl methyl cellulose having average molecular weight of approximately 11,300 per mole, 5.0 grams of red ferric oxide, and 5.0 grams of magnesium stearate.

DESCRIPTION OF METHOD OF PERFORMING THE INVENTION

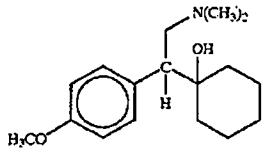
Additional embodiments of the invention pertains to a method for delivering a drug embraced by the structural formula of this invention for its intended therapy. One embodiment pertains to a method for delivering a drug of the formula by administering a dosage form comprising 0.5 mg to 750 mg of the drug from a dosage form selected from sustained-release and controlled-release dosage forms in a therapeutically responsive dose over an extended period of time. Another embodiment of the invention pertains to a method for delivering a drug of the formula disclosed in this invention, to the gastrointestinal tract of a human in need of this therapy, wherein the method comprises the steps of: (A) admitting orally into the gastrointestinal tract of the human a dosage form comprising: (1) a non-toxic wall composition comprising means for imbibing an external aqueous fluid through the wall into the dosage form, which wall surrounds and defines; (2) an internal compartment; (3) a drug composition comprising a drug of the formula in the compartment comprising a dosage unit amount of said drug; (4) a push composition in the compartment for pushing the drug composition from the compartment; (5) at least one exit means in the wall for delivering the drug from the dosage form; (B) imbibing fluid through the wall into the compartment thereby causing the composition to form a deliverable dosage form and concomitantly causing the push composition to expand and push the drug composition through the exit means from the dosage form; and (C) deliver the therapeutic drug in a therapeutically effective amount at a controlled rate over an extended period of time to the patient in need of said therapy. The method also comprising dispensing a dose amount of said drug from an instant release exterior dosage amount of drug to the patient for providing instant anti-depressant therapy.

Inasmuch as the foregoing specification comprises preferred embodiments of the invention, it is understood that variations and modifications may be made herein, in accordance with the inventive principles disclosed, without departing from the scope of the invention.

We claim:

1. A method for administering a drug to the gastrointestinal tract of a human, wherein the method comprises:

(a) admitting orally into the human a dosage form comprising a drug of the formula:



which drug possess antidepressant therapy and the dosage form comprises a member selected from the group consisting of a sustained-release dosage form and a controlled-release dosage form; and,

(b) administering the drug from the dosage form over an extended period of time in a therapeutically responsive dose to produce the antidepressant therapy.

* * * * *

EXHIBIT 2

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 3

EXHIBIT REDACTED IN ITS ENTIRETY

EXHIBIT 4

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(57) Abstract

The invention pertains to a dosage form (10) and to administering an antidepressant medicament (16) for an extended period of time in a rate-known dose.

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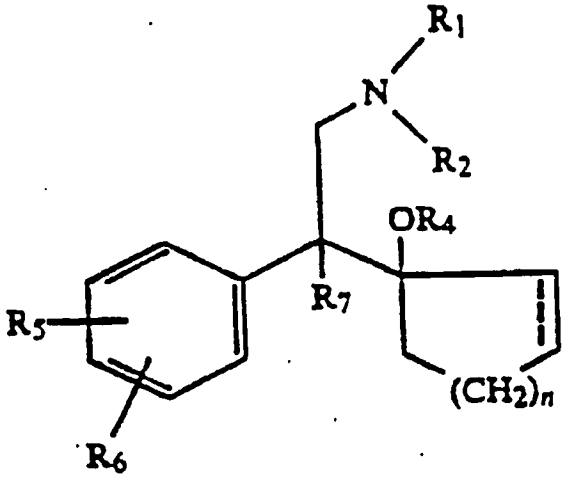
CH	Switzerland	KR	Republic of Korea	SI	Slovenia
CI	Côte d'Ivoire	KZ	Kazakhstan	SK	Slovakia
CM	Cameroon	LI	Liechtenstein	SN	Senegal
CN	China	LK	Sri Lanka	TD	Chad
CS	Czechoslovakia	LU	Luxembourg	TG	Togo
CZ	Czech Republic	LV	Latvia	TJ	Tajikistan
DE	Germany	MC	Monaco	TT	Trinidad and Tobago
DK	Denmark	MD	Republic of Moldova	UA	Ukraine
ES	Spain	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali	UZ	Uzbekistan
FR	France	MN	Mongolia	VN	Viet Nam
GA	Gabon				

ANTIDEPRESSANT DOSAGE FORM

FIELD OF THE INVENTION

This invention pertains to a controlled-release dosage form comprising a compound of the following structural formula:



useful for antidepressant therapy. The invention concerns also a method useful for antidepressant therapy by administering the controlled-release dosage form comprising the compound of the formula.

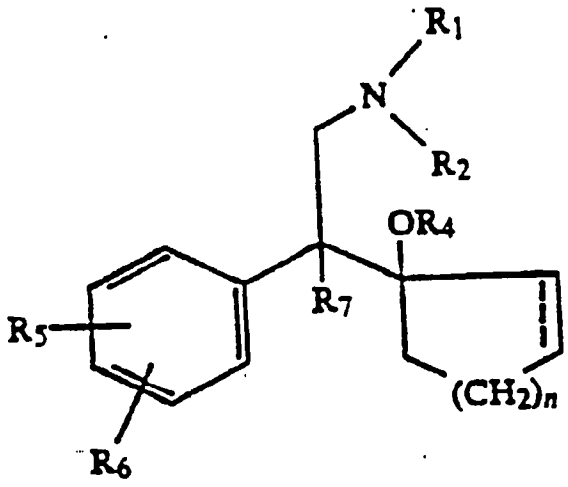
BACKGROUND OF THE INVENTION

The primary goal of drug administration is to provide a therapeutic dose of drug in the body to achieve a desired blood concentration, and then maintain the desired drug blood concentration. The prior art, in attempts to obtain the desired therapeutic effect, often used different dosage forms or programs. One dosage program consists of a single dosing of the drug from a conventional capsule or tablet that produced a

rapid rise followed by an immediate decline of the drug blood level versus time. The single dosing does not maintain the drug within a therapeutic range for an extended period of time, but exhibits of a short duration of action due to the inability of the conventional dosage form to provide drug delivery over time.

Another prior art dosing program used to obtain and to achieve drug blood levels consists in administering the drug repetitively using conventional dosage forms at various dosing intervals, as in multiple-dose therapy. In administering a drug according to the multiple-dose therapy, the drug blood level reached and the time required to reach that level depends on the dose and the dosing interval. There are, however, several potential problems inherent in multiple dose therapy. For example, if the dosing interval is not appropriate for the biological half-life of the drug, large peaks and valleys may result in the drug blood levels. Also, the drug blood level may not be within the therapeutic range at sufficiently early times, an important consideration for many disease states. And too, patient noncompliance with the multiple dosing regimen can result in a failure of this approach, especially as a drug in circulation surges to a high each time the drug is administered followed by a decline in drug concentration in the blood and in body compartments. Thus, a graph of drug in circulation following a dosage program of several doses, has an appearance of a series of peaks, which may surpass the toxic threshold. Then, each time the blood levels decreases into valleys, below a critical level needed to achieve a desired therapeutic effect, that effect may not be obtainable in the blood and body. Conventional dosage forms and their mode of operation are discussed in Remington's Pharmaceutical Sciences, 18th Edition, pages 1676 to 1686, (1990), Mack Publishing Co.; The Pharmacological Basis of Therapeutics, 7th Edition, page 7 (1985) published by MacMillian Publishing Co., and in United States Pat. Nos. 3,598,122 and 3,598,123 both issued to Zaffaroni.

A critical need exists for a controlled-rate dosage form for administering the drug of the formula:



which drug is presently administered in conventional dosage forms including tablets, capsules, elixirs and suspensions. These conventional dosage forms produce the peaks and valleys drug pattern presented above and they do not provide for controlled-rate therapy over an extended period of time. The drug of the formula is dosed twice or thrice a day now because of its elimination half-life of three to five hours. This pattern of dosing indicates the need for a controlled-release dosage form that can administer the drug at a controlled rate over an extended time to provide constant therapy and thereby eliminate the need for multiple

dosing. The drugs of the structural formula are known in United States Patent Nos. 4,535,186; 4,611,078; and 4,761,501 all issued to Husbands, Yardley and Muth.

The prior art provided controlled-release dosage forms that can continuously over time administer a drug for controlled-rate therapy. For example, in United States Pat. No. 4,327,725 issued to Cortese and Theeuwes and in United States Pat. Nos. 4,612,008; 4,765,989; and 4,783,337 issued to Wong, Barclay, Deters, and Theeuwes. The dosage forms disclosed in these patents provide a drug at a constant rate for effecting a therapeutic range for preferred therapy. The dosage forms of the patents provide a therapeutic range and avoids delivering the drug in excess in a toxic range with its accompanying side-effects. The dosage forms of the patents in providing a controlled dose in a therapeutic range also avoids delivering the drug in an ineffective dose in an ineffective range.

The dosage forms presented immediately above operate successfully for their intended use and they can deliver many drugs indicated for good therapy. The drugs of the above structural formula, however, possess properties such as a high solubility of 570 mg per ml at a body temperature of 37°C. that can lead to a premature release of the drug from the dosage form. During operation of the dosage forms, the convection motion of the imbibed fluid, and the hydrostatic pressure of the imbibed fluid coupled with the high solubility can result in the premature release of the drugs of the formula.

It is immediately apparent in the light of the above presentation that an urgent need exists for a dosage form endowed with controlled-release delivery for delivering the drugs embraced by the structural formula. The need exists for the dosage form for delivering the drug at a

controlled dose in a therapeutic range while simultaneously providing the intended therapy. It will be appreciated by those versed in the dispensing art, that such a dosage form that can administer the drug in a controlled-rate dose over time, would, represent an advancement and a valuable contribution to the art.

OBJECTS OF THE INVENTION

Accordingly, in view of the above presentation, it is an immediate object of this invention to provide a dosage from that possesses controlled-release delivery for providing a dosage form for administering a drug of the structural formula.

Another object of the present invention is to provide a dosage form for administering the drug of the formula in a controlled-rate dose in a therapeutic range over a prolonged period of time.

Another object of the present invention is to provide a dosage form that can deliver the drug of the formula essentially-free of a premature release from the dosage form.

Another object of the present invention is to provide a drug delivery controlled-release system that can deliver a drug for maintaining constant drug levels in the blood thereby functioning as a prolonged release system.

Another object of the present invention is to provide drug delivery sustained-release system that provides slow release of the drug over an extended period of time optionally in a therapeutic range.

Another object of the present invention is to provide a dosage form that substantially reduces and/or substantially eliminates the unwanted influences of a gastrointestinal environment of use and still provides controlled drug administration.

Another object of the present invention is to provide an improvement in a dosage form for administering a drug embraced by the structural formula and its pharmaceutically acceptable salt, wherein the improvement comprises delivering the drug in a controlled-release rate from the dosage form for improved and known therapy.

Another object of the invention is to provide a once-a-day controlled-release dosage form to deliver the drug of the structural formula orally to a patent in need of therapy.

Another object of the invention is to provide a method for administering a drug of the formula by orally administering the drug in a controlled rate dose per unit dose over an extended time to an animal in need of therapy.

Another object of the present invention is to provide a method for administering a drug of the formula in a therapeutic range while simultaneously substantially-avoiding a toxic range and an infective range.

Another object of the present invention is to provide a therapeutic composition comprising a drug of the structural formula blended with a drug-composition forming polymer.

Another object of the invention is to provide a therapeutic composition comprising a member selected from the group consisting of

venlafaxine and its pharmaceutically acceptable additional salt and a pharmaceutically acceptable polymer carrier for venlafaxine and its acceptable salts.

Other objects, feature, and advantages of the invention will more apparent to those versed in the dispensing arts from the following detailed specification, taken in conjunction with the drawings and the accompanying claims.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawing figures, which are not drawn to scale, but are set forth to illustrate various embodiments of the invention, the drawing figures are as follows:

Drawing Figure 1 is a general view of a dosage form provided by the invention, which dosage form is designed and shaped for oral administration, and for a drug delivery in a controlled-rate dose in the gastrointestinal tract;

Drawing Figure 2 is an opened view of the dosage form of drawing Figure 1 for depicting the structure of the dosage form and the composition member contained inside the dosage form; and

Drawing Figure 3 is a view of a dosage form that depicts an external, instant-release of drug of the structural formula coated on the exterior surface of the dosage form.

In the drawing figures, and in the specification, like parts in related figures are identified by like numbers. The terms appearing earlier in the

specification and in the description of the drawing figures, as well as embodiments thereof, are further described elsewhere in the disclosure.

DETAILED DESCRIPTION OF THE DRAWINGS

Turning now to the drawing figures in detail, which drawing figures are examples of dosage forms provided by this invention, and which examples are not to be construed as limiting, one example of a dosage form is seen in drawing Figure 1. In drawing Figure 1, a dosage form 10 is seen comprising a body member 11, which body 11 comprises wall 12, that surrounds and forms an internal area, not seen in drawing Figure 1. Dosage form 10 comprises at least one exit port 13 for connecting the exterior with the interior of dosage form 10.

The dosage form 10 of drawing Figure 1 illustrates a controlled-release dosage form manufactured as an osmotic dosage form that delivers a drug by osmotic action over an extended period of time. The dosage form comprising controlled-release properties embraced by this invention are successful at maintaining substantially constant drug levels in the blood or in a tissue. The dosage forms within the mode and manner of this invention comprises also sustained-release dosage forms. The sustained-release dosage forms releases the drug and provide drug levels in the blood or target tissue within a therapeutic range over an extended period of time. The invention embraces additionally prolonged release dosage forms. The prolonged release dosage form denotes extended duration of drug delivery action over that achieved by conventional drug delivery.

In drawing Figure 2, dosage form 10 of Figure 1 is seen in opened section. In drawing Figure 2, dosage form 10 comprises a body 11, a wall 12 that surrounds and defines an internal compartment 14. In

drawing Figure 2, internal compartment 14 communicates through an exit passageway 13 with the exterior of dosage form 10.

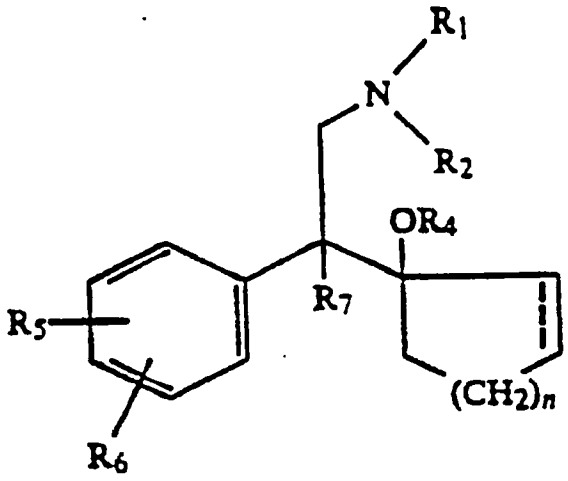
Wall 12 of dosage form 10 comprises totally or in at least a part of a composition that is permeable to the passage of an exterior fluid present in an environment of use, such as aqueous and biological fluids. Wall 12 is formed of nontoxic ingredients, is substantially impermeable to the passage of a drug and other ingredients present in compartment 14. Wall 12 comprises a composition that is substantially inert, that is, wall 12 maintains its physical and chemical integrity during the drug dispensing life of a drug from dosage form 10. The phrase, "maintaining its physical and chemical integrity," means wall 12 does not lose its structure and it does not change during the dispensing life of dosage form 10, except for possible leaching of one or more exit 13 passageway formed during operation of dosage form 10 or for leaching a water-soluble flux enhancers blended into wall 12. Wall 12 comprises a material that does not adversely affect an animal, a human or any other components comprising the dosage form. Representative materials for forming wall 12, are in one embodiment, a cellulose ester polymer, a cellulose ether polymer and a cellulose esterether polymer. These cellulosic polymers have a degree of substitution. D.S., on the anhydroglucose unit, from greater than 0 up to 3 inclusive. By degree of substitution is meant the average number of hydroxyl groups originally present on the anhydroglucose unit comprising the cellulose polymer that are replaced by a substituting group. Representative materials include a member selected from the group consisting of cellulose acylate, cellulose diacylate, cellulose triacylate, cellulose acetate, cellulose diacetate, cellulose triacetate, mono-, di- and tricellulose alkanylates, mono-,di-, and tricellulose aroylates, and the like. Exemplary polymers include cellulose acetate having a D.S. up to 1 and an acetyl content up to 21%; cellulose acetate having a D.S. of 1 to 2 and an acetyl content of 21 to 35 %;

cellulose acetate having a D.S. of 2 to 3 and an acetyl content of 35 to 44.8%, and the like. More specific cellulosic polymers include cellulose propionate having a D.S. of 1.8 and a propyl content of 39.2 to 45% and a hydroxyl content of 2.8 to 5.4%; cellulose acetate butyrate having a D.S. of 1.8, an acetyl content of 13 to 15% and a butyryl content of 34 to 39%; cellulose acetate butyrate having an acetyl content of 2 to 29%, a butyryl content of 17 to 53% and a hydroxyl content of 0.5 to 4.7; cellulose triacylates having a D.S. of 2.9 to 3 such as cellulose trivalerate, cellulose trilaurate, cellulose tripalmitate, cellulose trisuccinate, and cellulose trioctanoate; cellulose diacylates having a D.S. of 2.2 to 2.6 such as cellulose disuccinate, cellulose dipalmitate, cellulose dioctanoate, cellulose dipentanoate, co-esters of cellulose such as cellulose acetate butyrate and cellulose acetate propionate, and the like.

Additional polymers include ethyl cellulose of various degree of etherification with ethoxy content of from 40% to 55%, acetaldehyde dimethyl cellulose acetate, cellulose acetate ethyl carbamate, cellulose acetate methyl carbamate, cellulose acetate diethyl aminoacetate, semipermeable polyamides; semipermeable polyurethanes; semipermeable sulfonated polystyrenes; semipermeable cross-linked selective polymers formed by the coprecipitation of a polyanion and a polycation as disclosed in U.S. Pat Nos. 3,173,876, 3,276,586, 3,541,005; 3,541,006, and 3,546,142; semipermeable polymers as disclosed by Loeb and Sourirajan in U.S. Pat. No. 3,133,132; semipermeable lightly cross-linked polystyrene derivatives, semipermeable cross-linked poly(sodium styrene sulfonate); semipermeable cross-linked poly(vinylbenzyltrimethyl ammonium chloride); semipermeable polymers exhibiting a fluid permeability of 2.5×10^{-8} to 2.5×10^{-4} (cm^2/hr.atm) expressed per atmosphere of hydrostatic or osmotic pressure difference across the semipermeable wall. The polymers are known to the art in U.S. Pat. Nos. 3,845,770; 3,916,899; and 4,160,020; and in Handbook

of Common Polymers by Scott, J. R. and Roff, W. J., 1971 published by CRC Press, Cleveland, OH.

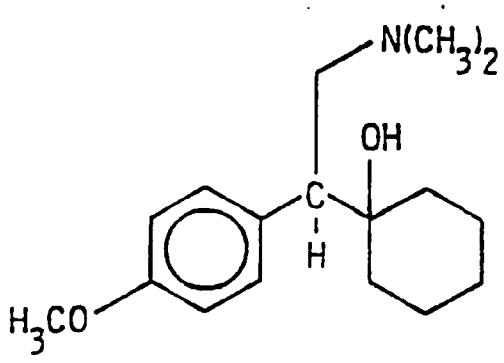
Compartment 14 comprises a drug composition, identified as drug layer 15 which contains drug 16, identified by dots. Drug 16 comprises a drug of the following structural formula:



wherein the dotted line represents optional unsaturation or a cycloalkenyl moiety; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl, an alkyl of 1 to 6 carbon atoms, an alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms in which each alkyl group comprises 1 to 6 carbon atoms, alkanamido of 2 to 7 carbon

atoms, halo, and trifluoroethyl, R_7 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbons, and n is one of the integers 0, 1, 2, 3, and 4. The formula embraces also the pharmaceutically acceptable addition salts including a member selected from the group consisting of inorganic, organic, hydrochloric, hydrobromic, gluconic, fumaric, maleric, sulfonic, succinic, sulfuric, phosphoric, tartaric, acetic, proponic, citric, oxalic and similar pharmaceutically acceptable addition salts. The compounds are known in U.S. Pat. Nos. 4,535,186; 4,611,078; 4,761,501; and 5,190,765.

The drugs of the structural formula are represented by the drug 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol of the structural formula:



The drug embraced by the formula possesses antidepressant properties. The drug in vitro prevents the neuronal uptake of serotonin, morepinephrine, and dopamine and it does not inhibit monoamine oxidase. The drug antagonizes reserpine-induced hypothermia and potentiates the effects of levodopa, and reduces histamine-induced

corticotropin release and induces cyclicadenosine monophosphate subsensitivity after both acute and chronic administration. The drug possesses excellent antidepressant activity in humans. The therapeutic amount of drug 16 in dosage form 10 is 0.5 mg to 750 mg, with individual dosage forms comprising 2, 5, 10, 25, 40, 50, 75, 100, 150, 250, 300, 500, and 600 mg of drug 16 for administering in a single dose or in more then one dose over an extended period of 24 hours. The therapeutic properties of the drug embraced by the structural formula are reported in Current Therapeutic Research, Vol. 42, No. 5, pages 901 to 909 (1987).

Composition 15 comprising drug 16 may comprise a drug dispensing carrier and composition formulating member consisting of a member selected from the group consisting of 0 wt% to 25 wt% of a hydroxypropylalkylcellulose where alkyl consists of 1 to 7 carbons selected from the group consisting of methyl, ethyl, isopropyl, butyl, pentyl, and hexyl which cellulose member comprises a 9,000 to 1,250,000 molecular weight and is exemplified by hydroxypropylmethylcelluose, hydroxypropylethylcellulose, hydroxypropylisopropylcellulose, hydroxypropylbutylcellulose and hydroxypropylhexylcellulose represented by dashes 17; a member selected from the group consisting of 0 wt% to 20 wt% hydroxylalkylcellulose where alkyl is 1 to 6 carbons including methyl, ethyl, propyl, butyl, pentyl, and hexyl which cellulose member comprises a 7,500 to 750,000 molecular weight and is exemplified by hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxyisopropylcellulose and hydroxybutylcellulose as represented by slanted line 18; a member selected from the group consisting of 0 wt% to 35 wt% of a vinyl-polymer having a 3,500 to 750,000 molecular weight represented by poly-n-vinylamide, poly-n-vinlycetamide, poly-n-vinylethylacetamide, poly-n-vinylmethylpropionamide, poly-n-vinyl

ethylpropionamide, poly-n-vinylmethylisobutyramide, poly-n-vinyl-2-pyrrolidone, poly-n-vinypiperidone also known as polyvinylpyrrolidone and as poly-n-vinylpyrroledone, poly-n-vinylcaprolactam, poly-n-vinyl-5-methyl-2-pyrrolidone and poly-n-vinyl-3-methyl-2-pyrrolidone, and poly-n-vinylpyrrolidone copolymer with a member selected from the group consisting of vinyl acetate, vinyl alcohol, vinyl chloride, vinyl fluoride, vinyl butyrate, vinyl laurate and vinyl stearate represented by small circles 19; and 0 wt%, where wt% is weight percent, 35 wt% of a maltodextrin polymer composition comprising the formula $(C_6H_{12}O_5)_n H_2O$ wherein n is 3 to 7,500 and the maltodextrin polymer comprises a 500 to 1,250,000 number average molecular weight represented by a small square 20; as member selected from the group consisting of 0 wt% to 40 wt% of poly(etheylen oxide) having a molecular weight of 100,000 to 600,000 grams per mole, represented by half-circles 20a. Composition 15 optionally comprises from 0 to 4.5 wt% of a lubricant represented by magnesium stearate, calcium stearate or stearic acid. The total weight of all ingredients in composition 15 is equal to 100 wt%, weight percent.

Compartment 14 comprises a displacement composition or push layer 21. Displacement composition 21 comprises a polymer member selected from the group consisting of a polymer possessing a repeating molecular unit $-(-O-CH_2CH_2-)_n$ wherein n is a positive whole number of 50,000 to 300,000 as represented by a poly(alkylene oxide) comprising poly(ethylene oxide) seen as wavy line 22; a maltodextrin polymer of the formula $(C_6H_{12}O_5)_n H_2O$ wherein n is 50 to 62,000 and comprises a 9,000 to 10,000,000 molecular weight and represented by triangle 23; a carboxymethylcellulose polymer comprising a 10,000 to 5,000,000 molecular weight represented by alkali carboxymethylcellulose, sodium carboxymethylcellulose and potassium carboxymethylcellulose, ammonium carboxymethylcellulose, sodium carboxymethyl-2-hydroxyethylcellulose, sodium carboxymethyl-methylcellulose, alkali

carboxymethyl-hydroxypropyl-methylcellulose, alkali carboxymethyl-2-hydroxyethylmethylcellulose, alkali carboxymethyl-2-hydroxybutylmethylcellulose, alkali carboxymethyl-2-hydroxyethyl-ethylcellulose and alkali carboxymethyl-2-hydroxypropylcellulose, where alkali is sodium and potassium and seen in drawing Figure 2 as hexagonal 23a. The polymers in push layer 21 provide unforeseen operating advantages as the polymer maintains its chemical composition during operation as it imbibes an external aqueous fluid including biological fluid while simultaneously pushing the drug from the dosage form essentially-free of substantially mixing the drug composition with the push composition. The displacement composition 21 comprises optionally from 4 to 35 wt% of an osmotically active compound, also known as osmagent and represented by vertical line 24. Representative of osmotically effective compounds comprises salts, oxides, esters that exhibit imbibition properties, carbohydrates and acids including a member selected from the group consisting of magnesium sulfate, magnesium chloride, sodium chloride, lithium chloride, potassium chloride, potassium sulfate, sodium sulfate, sodium sulfite, lithium sulfate, ammonium chloride, potassium lactate, mannitol, urea, magnesium succinate, tartaric acid, raffinose, sorbitol, sucrose, fructose, and glucose. Displacement layer 21 optionally comprises 0.5 wt % to 30 wt% of a cellulose polymer 25 represented by the letter v. Representative of cellulose polymer 25 comprise a member selected from the group consisting of hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxypropylethylcellulose, hydroxypropylisopropylcellulose, hydroxypropylbutylcellulose, hydroxypropylpentylcellulose, and hydroxypropylhexylcellulose comprising a 9,000 to 225,000 molecular weight. The displacement composition optionally comprises 0 wt% to 5 wt% of lubricant stearic acid and, magnesium stearate, calcium oleate, oleic acid, and caprylic acid. The polymers are known in U.S. Pat Nos.

3,845,770; and 4,160,020; in Handbook of Common Polymers by Scott, J. R., and Roff, W. J., published by CRC Press, Cleveland, OH.

Dosage form 10, a seen in drawing Figure 3 depicts another preferred manufacture provided by the invention. Dosage form 10, in drawing Figure 3, comprises an external coat on a the exterior surface of dosage form 10. Coat 26 is a therapeutic composition comprising 10 mg to 150 mg of drug 16, represented by dots 16. Exterior coat 26 provides instant drug 16 for instant therapy. Drug 16 is blended with an aqueous-soluble composition comprising a carrier methylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and blends of hydroxypropylcellulose and hydroxypropylmethylcellulose. Coat 26 optionally comprises polyethylene glycol or acetylated triglycerides. Coat 26 provides instant therapy as coat 26 dissolves or undergoes dissolution in the presence of a biological fluid and concurrently therewith delivers drug 16 to a drug receiving patient. Coat 26 provides instant therapy and it essentially overcomes the time required for the drug to be delivered from the dosage form.

Dosage form 10, as provided by this invention, and as seen in the above drawing figures can be manufactured for administering drug 16 by the oral route, and in another embodiment, dosage form 10 comprising exterior and interior drug 16 can be sized and shaped for administering drug 16 by the sublingual and buccal routes. The sublingual and buccal routes can be used for quicker therapy and they can be used when a smaller dose of drug 16 is needed for therapy. The buccal and sublingual routes can be used as a by-pass of the first pass of hepatic metabolism of drug 16. The sublingual or buccal routes can be used for administering the first dose of drug, followed by permitting dosage form 10 to enter the gastrointestinal tract for subsequent drug delivery.

Dosage form 10, when manufactured as an osmotic, controlled-release dosage form, comprises at least one passageway 13, or more than one passageway 13. The expression "at least one passageway" includes aperture, orifice, bore, pore, porous element through which the drug can be pumped, diffuse, travel or migrate, hollow fiber, capillary tube, porous overlay, porous insert, microporous member, porous composition, and the like. The expression also includes a material that erodes or is leached from wall 12 in the fluid environment of use to produce at least one passageway in dosage form 10. Representative material suitable for forming at least one passageway, or a multiplicity of passageways, includes an erodible poly(glycolic) acid or poly(lactic) acid member in the wall; a gelatinous filament; poly(vinyl alcohol); leachable materials such as fluid removable pore forming polysaccharides, salts, or oxides, and the like. A passageway or a plurality of passageways can be formed by leaching a material such as sorbitol, sucrose, lactose, fructose, or the like, from the wall to provide an osmotic dimensioned pore-passageway. The passageway can have any shape such as round, triangular, square, elliptical, and the like, for assisting in the metered release of drug from dosage form 10. Dosage form 10 can be constructed with one or passageways in spaced apart relation on one or more than a single surface of a dosage form. Passageways and equipment for forming passages are disclosed in U.S. Pat. Nos. 3,845,770 and 3,916,899 by Theeuwes and Higuchi; in U.S. Pat No. 4,063,064 by Saunders et al; and in U.S. Pat. No. 4,088,864 by Theeuwes et al. Osmotic passageways comprising controlled-drug releasing dimension, sized, shaped and adapted as a drug releasing pore formed by aqueous leaching to provide a drug-releasing pore of controlled osmotic release rate are disclosed in U.S. Pat. No. 4,200,098 by Ayer and Theeuwes; and in U.S. Pat. No. 4,285,987 by Ayer and Theeuwes.

Wall 12 of osmotic dosage form 10 can be formed in one technique using the air suspension procedure. This procedure consists in suspending and tumbling the compressed drug-push core laminate in a current of air and wall forming composition until a wall is applied to the drug-push compartment. The air suspension procedure is well-suited for independently forming the wall. The air suspension procedure is described in U.S. Pat. No. 2,799,241; J. Am. Pharm. Assoc., Volume 48, pages 451 to 454, (1959); and ibid, Volume 49, pages 82 to 84, (196). Osmotic dosage forms can also be coated with a wall forming composition in a Wurster ® air suspension coater, using methylene dichloride-methanol cosolvent, 80:20, wt:wt, an ethanol-water, or acetone-water cosolvent, 95:5 wt:wt using 2.5 to 4% solids. The Aeromatic ® air suspension coater using a methylene dichloride-methanol cosolvent, 80:20 wt:wt, also can be used for applying the wall. Other wall forming techniques such as pan coating system, where wall forming compositions are deposited by successive spraying of the composition on the drug-push compartment, accompanied by tumbling in a rotating pan. Finally, the wall coated compartments are dried in a forced air over at 30°C. to 50°C. for up to a week to free dosage form 10 of solvent. Generally, the walls formed by these techniques have a thickness of 2 to 30 mils with a presently preferred thickness of 4 to 10 mils.

Dosage form 10 of the invention is manufactured by standard manufacturing techniques. For example, in one manufacture the beneficial drug and other ingredients comprising the drug layer facing the exit means are blended and pressed into a solid layer. The drug and other ingredients can be blended with a solvent and mixed into a solid or semisolid formed by conventional methods such a ball-milling, calendering, stirring or rollmilling and then pressed into a preselected shape. The layer possesses dimensions that correspond to the internal dimensions of the area the layer is to occupy in the dosage form and it

also possesses dimensions corresponding to the second layer for forming a contacting arrangement therewith. Next, the push layer, is placed in contact with the drug layer. The push layer is manufactured using techniques for providing the drug layer. The layering of the drug layer and the push layer can be fabricated by conventional press-layering techniques. Finally, the two layer compartment forming members are surrounded and coated with an outer wall. A passageway is laser, leached, or mechanically drilled through the wall to contact the drug layer, with the dosage form optically oriented automatically by the laser equipment for forming the passageway on the preselected surface when a laser is used for forming the passageway.

In another manufacture, the dosage form is manufactured by the wet granulation technique. In the wet granulation technique, for example, the drug and the ingredients comprising the drug layer are blended using an organic solvent, such as isopropyl alcohol-ethylene dichloride 80:20 v:v (volume:volume) as the granulation fluid. Other granulating fluid such as denatured alcohol 100% can be used for this purpose. The ingredients forming the drug layer are individually passed through a 40 mesh screen and then thoroughly blended in a mixer. Next, other ingredients comprising the drug layer are dissolved in a portion of the granulation fluid, such as the cosolvent described above. Then the latter prepared wet blend is slowly added to the drug blend with continual mixing in the blender. The granulating fluid is added until a wet blend is produced, which wet mass then is forced through a 20 mesh screen onto oven trays. The blend is dried for 18 to 24 hours at 30°C. to 50°C. The dry granules are sized then with a 20 mesh screen. Next, a lubricant is passed through an 80 mesh screen and added to the dry screen granule blend. The granulation is put into milling jars and mixed on a jar mill for 1 to 15 minutes. The push layer is made by the same wet granulation

techniques. The compositions are pressed into their individual layers in a Manesty ® press-layer press.

Another manufacturing process that can be used for providing the compartment-forming composition layers comprises blending the powered ingredients for each layer independently in a fluid bed granulator. After the powered ingredients are dry blended in the granulator, a granulating fluid, for example, poly(vinyl-pyrrolidone) in water, or in denatured alcohol, or in 95:5 ethyl alcohol /water, or in blends of ethanol and water is sprayed onto the powders. Optionally, the ingredients can be dissolved or suspended in the granulating fluid. The coated powders are then dried in a granulator. This process granulates all the ingredients present therein while adding the granulating fluid. After the granules are dried, a lubricant such as stearic acid or magnesium stearate is added to the granulator. The granules for each separate layer are pressed then in the manner described above.

The dosage form of the invention is manufactured in another manufacture by mixing a drug with composition forming ingredients and pressing the composition into a solid lamina possessing dimensions that correspond to the internal dimensions of the compartment. In another manufacture the drug and other drug composition-forming ingredients and a solvent are mixed into a solid, or a semisolid, by conventional methods such as ballmilling, calendering, stirring or rollmilling, and then pressed into a preselected layer forming shape. Next, a layer of a composition comprising an osmopolymer and an optional osmagent are placed in contact with the layer comprising the drug. The layering of the first layer comprising the drug and the second layer comprising the osmopolymer and optional osmagent composition can be accomplished by using a conventional layer press technique. The wall can be applied by molding, spraying or dipping the pressed bilayer's shapes into wall forming

materials. Another and presently preferred technique that can be used for applying the wall is the air suspension coating procedure. The procedure consists in suspending and tumbling the two layers in current of air until the wall forming composition surrounds the layers. The air suspension procedure is described in U.S. Pat. No. 2,799,241; J. Am. Pharm. Assoc., Vol. 48 pp 451-454 (1979); and, ibid, Vol. 49, pp 82-84 (1960). Other standard manufacturing procedures are described in Modern Plastics Encyclopedia, Vol 46, pp 62-70 (1969); and in Pharmaceutical Science, by Remington, 14th Ed., pp 1626-1678 (1970), published by Mack Publishing Co., Easton, Pa.

Exemplary solvents suitable for manufacturing the wall, the laminates and laminae include inert inorganic and organic solvents final laminated wall. The solvents broadly include members selected for the group consisting of aqueous solvents, alcohols, ketones, esters, ethers, aliphatic hydrocarbons, halogenated solvents, cyclaliphatics, aromatics, heterocyclic solvents and mixtures thereof. Typical solvents include acetone, diacetone, alcohol, methanol, ethanol, isopropyl alcohol, butyl alcohol, methyl acetate, ethyl acetate, isopropyl acetate, n-butyl acetate, methyl isobutyl ketone, methyl propyl ketone, n-hexane, n-heptaene ethylene glycol monoethyl ether, ethylene glycol monoethyl acetate, methylene dichloride, ethylene dichloride, propylene dichloride, carbon tetrachloride, chloroform, nitroethane, nitropropane, tetrachoroethan, ethyl ether, isopropyl ether, cyclohexane, cyclooctane, benzene, toluene, naphtha, tetrahydrofuran, diglyme, aqueous and nonaqueous mixtures thereof, such as acetone and water, acetone and methanol, acetone and ethyl alcohol, methylene dichloride and methanol, and ethylene dichloride and methanol.

DETAILED DISCLOSURE OF EXAMPLES OF THE INVENTION

The following examples are merely illustrative of the present invention and they should not be considered as limiting the scope of the invention in any way as these examples and other equivalents thereof will become apparent to those versed in the art in the light of the present disclosure, the drawings and accompanying claims.

EXAMPLE 1

A dosage form adapted for delivering a drug in a therapeutic range is manufactured as follows: first a displacement or push layer is prepared by blending and passing through a stainless steel sizing screen having a mesh opening of 420 microns 587.5 grams of sodium carboxymethylcellulose having a degree of polymerization of approximately 3,200 and a degree of substitution of 0.7 carboxymethyl groups per anhydroglucose unit, 300 grams of powdered sodium chloride, 50 grams of hydroxypropylcellulose having a molecular weight of approximately 60,000 grams per mole, and 50 grams of hydroxypropylmethylcellulose having an average methoxyl content of 29 weight percent and an average hydroxypropyl content of 10 weight percent and an average molecular weight of approximately 11,300 grams per mole. Next 10 grams of red ferric oxide were passed through a sizing screen having openings of approximately 250 microns. The resulting powders were mixed in a planetary mixer to a uniform blend. The resulting blend was wet granulated by adding with stirring anhydrous ethyl alcohol until, a cohesive mass was formed. This mass was passed through a sizing screen having openings of approximately 840 microns, forming coated displacement particles, which were an dried overnight at ambient temperature and humidity. The dried particles were then passed again through the 840 micron sizing screen. Next 2.5 grams of

magnesium stearate, which had been previously sized through a mesh having 180 micron openings, were tumble mixed into the coated particles.

A composition comprising a drug of the structural formula was prepared as follows: first, a drug composition was prepared by passing 840 grams of venlafaxine hydrochloride, 100 grams of hydroxypropylcellulose having a molecular weight of approximately 60,000 grams per mole, and 50 grams of polyvinylpyrrolidone having a molecular weight of approximately 40,000 grams per mole, were passed through a sizing having openings of approximately 420 microns, and mixed in a planetary mixer to yield a uniform blend. Then, anhydrous ethyl alcohol was added to the mixture with stirring to produce a cohesive damp mass. The resulting damp mass was sized through a sieve having an opening of 840 microns, producing coated venlafaxine drug, which was air dried overnight. The resulting dried coated venlafaxine drug was passed again through the sizing screen having an 840 micron opening. Next, 10 grams of magnesium stearate, sized to 180 microns, was tumble mixed into the blend.

Next, the displacement-push composition and the drug composition were formed into a bilayer core as follows: first, 87 mg of the drug composition was placed in a 9/32 inch round die cavity and lightly tamped with a standard concave round tooling to form a slightly cohesive layer. Then, 70 mg of push composition was added to die and the and the resulting fill was compressed with a final force of 2 tons, thereby forming a two layer cores.

The bilayer cores were placed next in a coating pan having a 12 inch diameter and they were coated with a wall-forming solution. The wall-forming solution was prepared by dissolving 380 grams of cellulose

acetate having an acetyl content of 39.8 weight percent in 7,220 grams of acetone. In a separate mixing vessel, 20 grams of polyethylene glycol having a molecular weight of approximately 3,350 grams per mole were dissolved in approximately 380 grams of purified water. The two solutions were mixed to form the wall-coating solution which was spray coated onto the cores until about 20 mg of wall composition was deposited on the surfaces of the bilayer core.

A delivery exit port was formed across the wall by drilling an exit port, centered on the face of the dosage form on the drug composition side of the dosage form. The resulting dosage form was placed in simulated physiological fluid at 37°C., and the dosage form delivered a dose of 73 mg of venlafaxine hydrochloride at a controlled, zero rate over an extended duration of 15 hours.

EXAMPLE 2

The procedure of Example 1 was followed with the manufacturing procedures as set forth, except that the drug composition comprises 890 grams of venlafaxine hydrochloride, 100 grams of hydroxypropylcellulose, and 10 grams of magnesium stearate. The resulting dosage form released in simulated intestinal fluid 77 mg of venlafaxine hydrochloride at a zero-order rate over an extended duration of 16 hours.

EXAMPLE 3

The procedure of Example 1 was followed with all manufacturing steps as described, except that the drug composition consists of 650.0 grams of venlafaxine hydrochloride, 240.0 grams of maltodextrin having an average molecular weight of approximately 1800 grams per mole and an average degree of polymerization of 11.1, 80.0 grams of

hydroxypropyl cellulose, 20.0 grams of polyvinyl pyrrolidone, and 10.0 grams of magnesium stearate. The resulting dosage form was tested in artificial intestinal fluid, the dosage form delivered a dose of 57 mg of venlafaxine hydrochloride at zero order rate over a period of 15 hours.

EXAMPLE 4

The procedure of Example 1 was repeated with the manufacture as previously set-forth, except that the drug composition consists of 840.0 grams of venlafaxine hydrochloride, 150.0 grams of polyethylene oxide having an average molecular weight of approximately 100,000 grams per mole, and 10.0 grams of magnesium stearate. The wall weight weighed approximately 25 mg. The resulting dosage forms were tested in simulated intestinal fluid, and they released a dose of 73 mg of venlafaxine hydrochloride at controlled rate over an extended period of 20 hours.

EXAMPLE 5

The compositions were manufactured as in Example 1. The process of manufacture was the same except that the push layer manufactured was prepared in a fluid bed aqueous-based granulation process. This was accomplished by sizing the sodium carboxymethyl cellulose, the sodium chloride, the hydroxypropyl cellulose, and red ferric oxide through a screen having openings of 420 microns. The resulting powders were charged into a fluid bed granulation column and binder solution consisting of the hydroxypropyl methylcellulose at a 5 percent solids concentration in water was sprayed on, thereby forming the granules for the push layer.

EXAMPLE 6

The compositions and processes followed in this example were the same as in Example 1 except the push consisted of 740.0 grams polyethylene oxide with an average molecular weight of approximately 5 million grams per mole, 200.0 grams of sodium chloride, 50.0 grams of hydroxypropyl methyl cellulose having average molecular weight of approximately 11,300 per mole, 5.0 grams of red ferric oxide, and 5.0 grams of magnesium stearate.

DESCRIPTION OF METHOD OF PERFORMING THE INVENTION

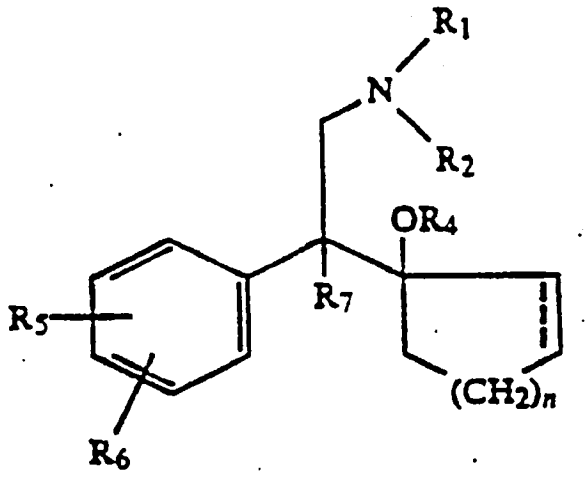
Additional embodiments of the invention pertains to a method for delivering a drug embraced by the structural formula of this invention for its intended therapy. One embodiment pertains to a method for delivering a drug of the formula by administering a dosage form comprising 0.5 mg to 750 mg of the drug from a dosage form selected from sustained-release and controlled-release dosage forms in a therapeutically responsive dose over an extended period of time. Another embodiment of the invention pertains to a method for delivering a drug of the formula disclosed in this invention, to the gastrointestinal tract of a human in need of this therapy, wherein the method comprises the steps of: (A) admitting orally into the gastrointestinal tract of the human a dosage form comprising: (1) a non-toxic wall composition comprising means for imbibing an external aqueous fluid through the wall into the dosage form, which wall surrounds and defines; (2) an internal compartment; (3) a drug composition comprising a drug of the formula in the compartment comprising a dosage unit amount of said drug; (4) a push composition in the compartment for pushing the drug composition from the compartment; (5) at least one exit means in the wall for delivering the drug from the dosage form; (B) imbibing fluid through the wall into the

compartment thereby causing the composition to form a deliverable dosage form and concomitantly causing the push composition to expand and push the drug composition through the exit means from the dosage form; and (C) deliver the therapeutic drug in a therapeutically effective amount at a controlled rate over an extended period of time to the patient in need of said therapy. The method also comprising dispensing a dose amount of said drug from an instant release exterior dosage amount of drug to the patient for providing instant anti-depressant therapy.

Inasmuch as the foregoing specification comprises preferred embodiments of the invention, it is understood that variations and modifications may be made herein, in accordance with the inventive principles disclosed, without departing from the scope of the invention.

We claim:

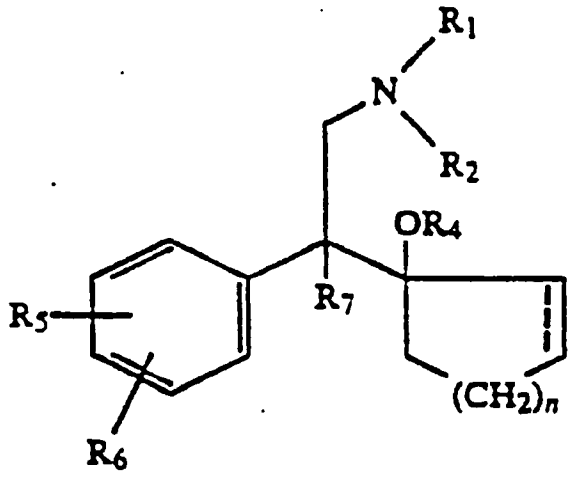
1. A therapeutic composition comprising 0.5 mg to 750 mg of a drug of the formula:



wherein the dotted line represents an unsaturation or a cycloalkenyl group; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl, an alkyl of 1 to 6 carbon atoms, an alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms in which each alkyl group comprises 1 to 6 carbon atoms, alkanamide of 2 to 7 carbon atoms, halo, and trifluoroethyl, R_7 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbons, and n is one of the integers 0, 1, 2, 3, and 4, and a pharmaceutically acceptable addition

salt; and wherein the drug of the formula is blended with a poly(alkylene oxide) polymer.

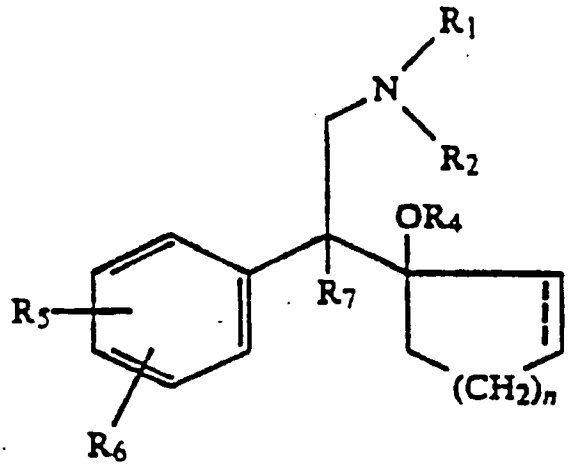
2. A therapeutic composition comprising 0.5 mg to 750 mg of a drug of the formula;



wherein the dotted line represents an unsaturation or a cycloalkenyl group; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl, an alkyl of 1 to 6 carbon atoms, an alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms in which each alkyl group comprises 1 to 6 carbon atoms, alkanamido of 2 to 7 carbon atoms, halo, and trifluoroethyl; R_7 is a member selected from the group

consisting of hydrogen and alkyl of 1 to 6 carbons and n is one of the integers 0, 1, 2, 3, 4, and a pharmaceutically acceptable addition salt; and wherein the drug of the formula is blended with a cellulose polymer.

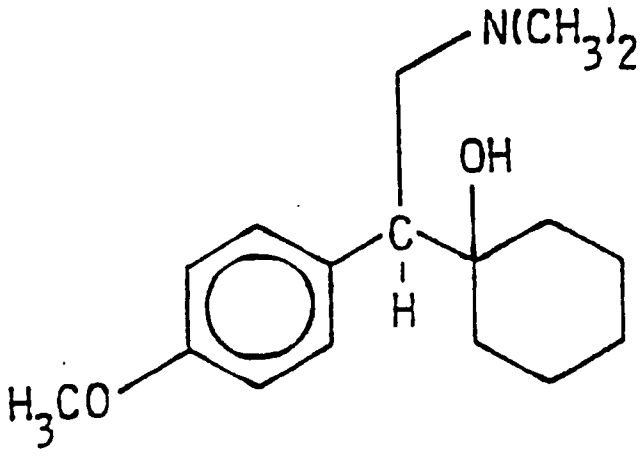
3. A therapeutic composition comprising 0.5 mg to 750 mg of a drug of the formula:



wherein the dotted line represents an unsaturation or a cycloalkenyl group; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl, an alkyl of 1 to 6 carbon atoms, an alkoxy of 1 to 6 carbon atoms, alkanoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6

carbon atoms, amino, alkylamino of 1 to 6 carbon atoms in which each alkyl group comprises 1 to 6 carbon atoms, alkanamido of 2 to 7 carbon atoms, halo, and trifluoroethyl, R_7 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbons, and n is one of the integers 0, 1, 2, 3, and 4; and a pharmaceutically acceptable addition salt; and wherein the drug of the formula is blended with a maltodextrin polymer.

4. A dosage form for administering a drug to an environment of use, wherein the dosage form comprises a drug of the formula:



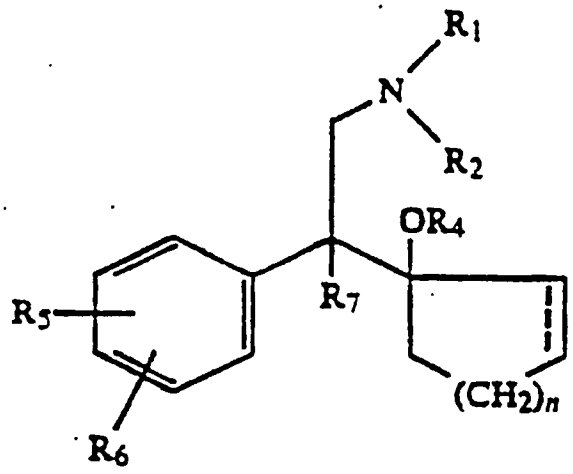
which dosage form comprises a member selected from the group consisting of a sustained-release dosage form and a controlled release dosage form, and wherein said dosage form comprises means for storing the drug and means for releasing the drug over an extended period of time.

5. A dosage form for the oral delivery of a drug to an environment of use, wherein the dosage form comprises:

(a) a wall comprising at least in part a composition permeable to the passage of fluid, which wall surrounds:

(b) a compartment;

(c) a drug composition in the compartment comprising a drug of the formula:



wherein the dotted line represents a member selected from the group consisting of an unsaturation and cycloalkenyl group; R_1 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_2 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbon atoms; R_4 is a member selected from the group consisting of hydrogen, alkyl of 1 to 6 carbon atoms, formyl, and alkanoyl of 2 to 7 carbon atoms; R_5 and R_6 are independently a member selected from the group consisting of hydrogen, hydroxyl and alkyl of 1 to 6 carbon atoms, alkoxy of 1 to 6 carbon atoms, alknaoyloxy of 2 to 7 carbon atoms, nitro, alkylmercapto of 1 to 6 carbon atoms, amino, alkylamino of 1 to 6 carbon atoms, alkanamido of 2 to 7 carbon atoms, halo and trifluoroethyl; R_7 is a member selected from the group consisting of hydrogen and alkyl of 1 to 6 carbons; an n is 0 to 4; and

(d) a displacement in the compartment comprising a composition comprising an osmotically active compound; and,

(e) an exit passageway in the dosage form for delivering the drug composition from the dosage form.

6. A dosage form for the oral delivery of the drug to an environment of use according to claim 5, wherein the drug is 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]-cyclohexanol.

FIG.1

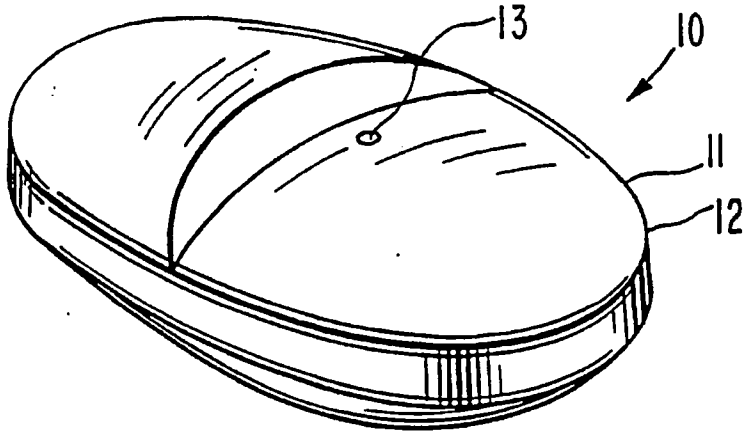


FIG.2

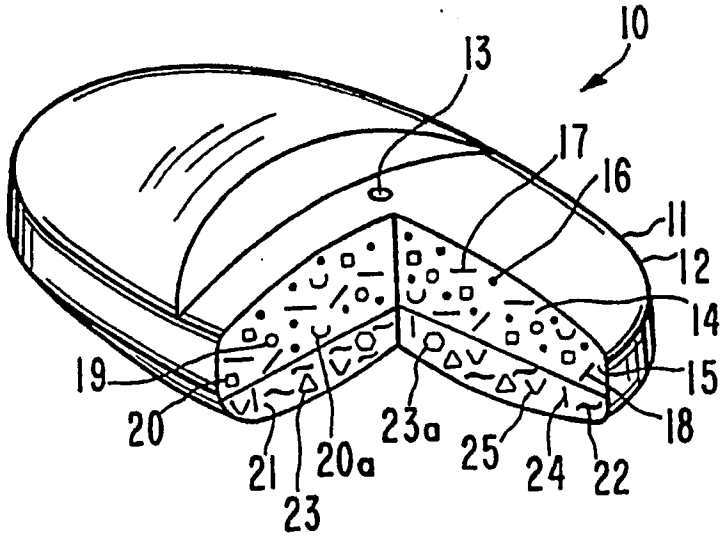


FIG.3

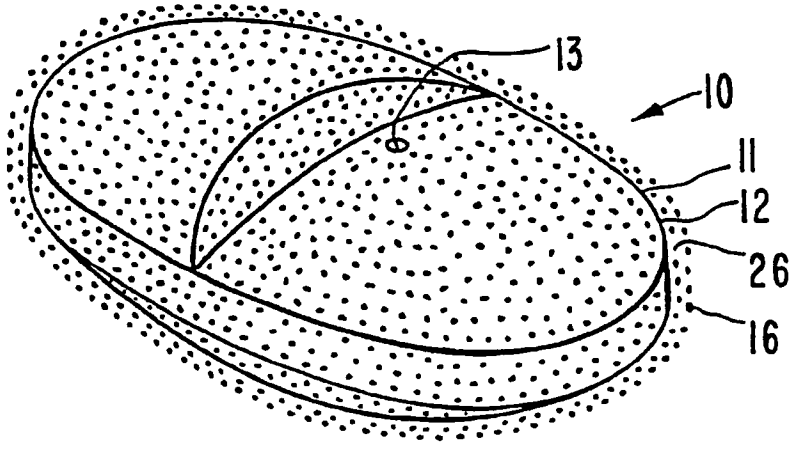


EXHIBIT 5

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH, Plaintiff, v. IMPAX LABORATORIES, INC., Defendant.	C. A. No. 06-222 (JJF)

PLAINTIFF'S RESPONSES AND OBJECTIONS TO IMPAX'S THIRD REQUEST FOR PRODUCTION OF DOCUMENTS AND THINGS (NOS. 87-124)

Plaintiff, Wyeth, hereby responds to the Third Request for Production of Documents and Things (Nos. 87-124) served by Defendant Impax Laboratories, Inc. (hereinafter "Impax") on September 8, 2006 via hand delivery.

GENERAL OBJECTIONS

1. Wyeth objects to any request to the extent it seeks to impose on Wyeth any obligation not required by the Federal Rules of Civil Procedure or the local rules of the United States District Court for the District of Delaware.

2. Wyeth objects generally to the production of documents and things protected by the attorney-client privilege, work product immunity, or any other applicable privilege. To the extent that such documents and things not otherwise objectionable are called for by Impax's requests, they will be identified in a listing of withheld documents which will be prepared in due course and exchanged with Impax on a mutually agreed upon date.

3. An objection based on attorney-client privilege and/or work product immunity should not be construed as a representation that such documents exist or existed. Such objections indicate only that the requests are of such a scope as to embrace subject matter protected by the attorney-client privilege and/or work product immunity.

4. Wyeth objects generally to Impax's document requests to the extent they seek production of documents and things containing both discoverable and nondiscoverable or objectionable material. Wyeth reserves the right to redact any matter which is not called for or with respect to which Wyeth has objected to the request for production.

5. Wyeth objects to Impax's instructions to the extent they include within the definition of Wyeth's possession, custody or control all documents to which Wyeth has any access, however remote. Thus, Wyeth objects to Impax's document requests to the extent they seek to require Wyeth to provide any information beyond what is available to Wyeth at present from a reasonable search of its own files at its principal offices and pharmaceutical product research and development facilities in the United States and from reasonable inquiry of its present employees on the grounds that such discovery is irrelevant, unreasonably cumulative and unduly burdensome. Subject to these objections, Wyeth will use reasonable diligence to locate responsive documents in its possession, custody, and control based on an examination of those files reasonably expected to yield responsive documents.

6. As used in these responses, the phrase "all documents," or similar phrases, should be understood to mean those documents Wyeth and its counsel were

able to locate using reasonable diligence and judgment concerning the existence and whereabouts of responsive documents. Such phraseology should not be construed as a representation that each and every document available to Wyeth has been examined in connection with these responses or any production pursuant thereto.

7. Wyeth's objections and responses are based on the best knowledge and information known to them at this time. Wyeth's objections and responses are made without prejudice to Wyeth's right to revise or supplement them based on the discovery taken in this case. Further, Wyeth's objections and responses are based on Wyeth's good-faith interpretation of the individual requests for production and are subject to correction for errors or omission, if any.

8. Wyeth objects to the production of documents in the public domain because the burden of obtaining access to, copying, and production is equal for both parties. Subject to this General Objection, and to the extent not otherwise objectionable, Wyeth will not seek to exclude from production, responsive public documents within its possession, custody, and control.

9. A response that documents will be produced should not be construed as a representation that such documents exist or existed. Such responses indicate only that documents responsive to the request, subject to applicable objections, will be produced if any such documents are found after a reasonable search.

10. To the extent that Impax's document requests seek the production of internal work product files from any of Wyeth's counsel, including, but not limited to, Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P. and Morris, Nichols, Arsht &

Tunnell, L.L.P., Wyeth objects to either the production or the listing of these documents on a withheld document list.

11. Wyeth objects to the production of documents and things subject to the rights of third parties not affiliated with Wyeth. In addition, Wyeth objects to the production of non-Wyeth documents or information subject to a protective order entered in a litigation other than the above-captioned litigation.

12. Wyeth objects to Impax's definition of the terms "Wyeth" or "Plaintiff." This action involves Wyeth and not its past or present, U.S. or foreign subsidiaries, past or present, U.S. or foreign divisions, or "any related companies." In addition, Wyeth objects to Impax's definition of "Wyeth" or "Plaintiff" to the extent these terms include former officers, directors, employees, agents, attorneys or representatives as potentially including entities outside of Wyeth's possession, custody, or control, and as calling for information that may be subject to confidentiality agreements and/or attorney-client privilege. Consequently, in answering Impax's requests, Wyeth will construe "Wyeth" and "Plaintiff" to mean only those portions of Wyeth involved with the research and development, manufacture, distribution, and/or sale of the venlafaxine hydrochloride extended release product EFFEXOR® XR in the United States. Wyeth further objects to Impax's instructions as unduly burdensome to the extent they seek to impose any further limitations or obligations upon Wyeth with respect to the production of documents within Wyeth's possession, custody, or control other than those set forth above.

13. Wyeth objects to the production of "electronically produced, electronically stored, photostatic, photographed, recorded, or otherwise reproduced communications

or records of every kind and description," documents as well as "computer files, including backup OR archival copies" as overly broad, unreasonably cumulative and unduly burdensome. Subject to the General and Specific Objections, Wyeth will agree to produce TIFF images of documents produced by Wyeth in the *Wyeth v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries, Ltd.* litigation, Civil Action No. 03-CV-1293 (WJM) (hereinafter "Teva litigation") that were obtained from searches of Wyeth's relevant electronic systems, assuming that Impax is willing to provide its produced documents, electronic or otherwise, to Wyeth in TIFF format, and that Impax reimburses Wyeth for half of the cost of imaging copies of documents previously imaged for the Teva litigation and for the full cost of imaging copies of any documents produced solely in this litigation. Alternatively, Wyeth is willing to produce documents to Impax in hard paper copy format and Impax can reimburse Wyeth for the cost of those copies.

14. Wyeth objects to Impax's requests to the extent they call for information (including listing on a withheld document log) or documents generated subsequent to the February 10, 2003 cut-off date observed in the Teva litigation as irrelevant, overly broad, unduly burdensome and not reasonably calculated to lead to the discovery of admissible evidence. The production or listing on a withheld document log of any document or information generated subsequent to this date should not be construed as a waiver of this objection with respect to any other document or information.

15. Wyeth objects to the production of documents relating to ongoing clinical trials that are not complete and/or not decoded, analyzed, or reported. Wyeth further objects to the production of information such as voluminous raw data and data

compilations from *in vitro* testing, pre-clinical studies, or clinical trials as unduly burdensome, unreasonably cumulative, unreasonably duplicative and irrelevant.

16. Wyeth objects to the production of commercial, financial, regulatory, marketing, patent prosecution and proceedings, legal and other documents to the extent they concern countries other than the United States as unduly burdensome, overly broad, and/or irrelevant to any issue in the suit, and not reasonably calculated to lead to the discovery of admissible evidence.

17. Wyeth objects to the production of routine manufacturing, production, qualification, quality control, quality assurance, batch records, release records, and other routine testing as overly broad, irrelevant, unduly burdensome, unreasonably cumulative and duplicative, and not reasonably calculated to lead to the discovery of admissible evidence.

18. The incidental production of any document or information covered by any of Wyeth's General or Specific Objections shall not be construed as a waiver of the objection with respect to any other document or information.

19. Nothing in these responses should be construed as waiving rights or objections which otherwise might be available to Wyeth, nor should Wyeth's answering any discovery request be deemed an admission of relevancy, materiality or admissibility in evidence of the discovery requests or the responses thereto.

20. The General Objections apply to all of Impax's Document Request Nos. 87-124. To the extent that specific General Objections are cited herein in response to specific document requests, those specific citations are provided because they are believed to be particularly applicable to the request and are not to be construed as a

waiver of any other General Objections applicable to documents falling within the scope of the request.

21. Wyeth maintains the General and Specific Objections it made in response to requests for production propounded by Defendants in the Teva litigation and hereby incorporates by reference herein all of those General and Specific Objections and Responses.

22. Although Wyeth objects generally to Impax's request that documents and things be produced at the offices of Heller Ehrman, LLP, Wyeth will forward to the offices of Heller Ehrman, LLP copies of produced documents with the understanding that Heller Ehrman, LLP will promptly reimburse Wyeth for the cost of those copies and that Impax will similarly forward its produced copies to the offices of Finnegan Henderson. Nevertheless, Wyeth retains the right to produce documents or things by making them available for inspection and copying by Impax at Wyeth's or Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.'s facilities.

23. Until a protective order is entered in this litigation any production of Wyeth's confidential documents is on an outside counsel eyes only basis pursuant to D. Del. L.R. 26.2.

24. Wyeth objects to Impax's Instructions to the extent they seek to impose on Wyeth obligations not required by the Federal Rules of Civil Procedure or the local rules of the United States District Court for the District of Delaware and as overly burdensome.

25. Wyeth objects to Impax's definition of "named inventors" to the extent it encompasses persons beyond Deborah M. Sherman, John C. Clark, John U. Lamer

and Stephen A. White as vague and ambiguous, overly broad, unduly burdensome, and irrelevant to any issue in the suit.

RESPONSES

IMPAX DOCUMENT REQUEST NO. 87:

DOCUMENTS sufficient to identify all electronic systems and databases, including without limitation, their location, the extent to which they are text-searchable, the extent to which they separately have fields and codes for metadata such as date, location, author, recipient, custodian, etc., used or maintained by WYETH or its attorneys that store any electronic media, including without limitation, e-mail, e-mail attachments, word processing files, spreadsheet files, files of scanned DOCUMENTS, PDF files, graphics files, compressed files, CONCERNING the PATENTS IN SUIT, the NAMED INVENTORS, EFFEXOR, EFFEXOR XR, EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE, NDA 20-699, clinical studies 600B-208-US, 600B-209-US, and 600B-367-EU, or the legal action entitled *Wyeth v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd.*, Civil Action No. 03-CV-1293 (WJM) before the United States District Court for the District of New Jersey.

OBJECTION:

Wyeth objects to this request to the extent it calls for documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth also objects to this request as overly broad, unduly burdensome, vague and ambiguous, and not reasonably calculated to lead to the discovery of admissible evidence to the extent that it seeks the identification of "all electronic systems and databases" and "any electronic media" that contain any information concerning the topics listed, however routine, trivial, or remote the information may be to any claim or defense in this litigation. For example, Wyeth further objects to this request as overly broad, vague and ambiguous, unduly burdensome, and not reasonably calculated to

lead to the discovery of admissible evidence to the extent it seeks information regarding the identification of databases regarding routine testing, ordering, production, quality control, distribution, personnel management, marketing, accounting, or other such routine manufacturing, logistics, human resources, or business information.

Wyeth further objects to this request as overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence to the extent the document request calls for information concerning "Wyeth", as that term is defined by Impax for the reasons set forth in Wyeth's General Objection No. 12, above. This action involves Wyeth and not its past or present, U.S. or foreign subsidiaries, past or present, U.S. or foreign divisions, past or present, U.S. or foreign parent corporations, or "any related companies." Nor does "Wyeth" reasonably include former officers, directors, employees, agents, attorneys, and representatives as potentially including entities outside of Wyeth's possession, custody, or control, or calls for documents that may be subject to confidentiality agreements and/or attorney-client privilege. Consequently, in answering this document request, Wyeth will construe "Wyeth" to mean only those portions of Wyeth involved with the research and development, manufacture, distribution, and/or sale of the venlafaxine hydrochloride extended release product EFFEXOR® XR in the United States. Wyeth further objects to Impax's instructions as unduly burdensome to the extent they seek to impose any further limitations or obligations upon Wyeth with respect to the production of information or documents within Wyeth's possession, custody, or control than those set forth above.

Wyeth further objects to this document request to the extent it uses Impax's definition of "named inventors" encompassing persons beyond Deborah M. Sherman,

John C. Clark, John U. Lamer and Stephen A. White as vague and ambiguous, overly broad, unduly burdensome, and irrelevant to any issue in the suit. Wyeth further objects to this document request to the extent it seeks information concerning any venlafaxine-containing extended release formulation developed after the effective filing date of the patents-in-suit, other than EFFEXOR® XR, as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information. Wyeth also objects to this request to the extent it seeks documents and things concerning "EFFEXOR" other than documents reflecting (1) comparisons between immediate release Effexor® and Effexor® XR or (2) nausea and/or vomiting in humans associated immediate release Effexor® as overly broad and unduly burdensome. Wyeth further objects to this request as overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence to the extent it calls for identification of documents concerning the identified databases beyond those that are ascertainable by a reasonable search.

Wyeth also objects to this document request to the extent that the terms "text searchable," "fields and codes for metadata" and "metadata" are vague and ambiguous. "Text searchable" does not define the extent to which any or all fields in a database are, in fact, searchable, or under what conditions such searches may occur. For purposes of responding to this request, therefore, Wyeth will consider a database as "text searchable" if at least one field may be searched for text during the course of a normal business application of that database. Similarly, "fields and codes for metadata" shall

be construed to refer to metadata that can be accessed using the program(s) commonly used to access that system or database in the normal course of business.

Finally, Wyeth's obligations concerning electronic document production including the production of metadata is the subject of a pending motion to compel. Therefore, Wyeth objects to this document request's request for information concerning metadata fields or codes as overly broad, unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence. Wyeth reserves the right to further supplement this response.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce a document containing Wyeth's response to Impax's Interrogatory No. 20.

IMPAX DOCUMENT REQUEST NO. 88:

All business plans CONCERNING EFFEXOR XR.

OBJECTION:

Wyeth objects to this request as overly broad, vague and ambiguous, unduly burdensome, not reasonably calculated to lead to the discovery of admissible evidence, and as seeking highly sensitive future competitive information. Impax has not defined "business plans" nor has it provided any nexus between the need for such documents and their relevance to any claim or defense in this litigation. Wyeth further objects to this request to the extent it calls for information (including listing on a withheld document log) or documents generated subsequent to the February 10, 2003 cut-off date

observed in the Teva litigation as irrelevant, overly broad, unduly burdensome and not reasonably calculated to lead to the discovery of admissible evidence.

Wyeth further objects to this request to the extent it calls for information that is protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or is otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 89:

All DOCUMENTS provided to physicians CONCERNING the characteristics and benefits of EFFEXOR XR.

OBJECTION:

Wyeth objects to this request to the extent it seeks "ALL Documents provided to physicians" as overly broad, vague and ambiguous, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence. Impax has not provided any nexus between the need for "all" such documents and their relevance to any claim or defense in this litigation.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva

litigation. In addition, Wyeth will produce additional, more recent advertising for its Effexor® XR products.

IMPAX DOCUMENT REQUEST NO. 90:

To the extent WYETH contends, or will contend in the event the Court adopts the claim constructions that were found in *Wyeth v. Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd.*, Civil Action No. 03-CV-1293 (WJM), that IMPAX infringes any asserted claim of the PATENTS IN SUIT under the doctrine of equivalents, DOCUMENTS CONCERNING WYETH's allegation that IMPAX'S VENLAFAXINE HYDROCHLORIDE EXTENDED RELEASE CAPSULE has an equivalent element, performs an equivalent step, or induces performance of an equivalent step, including without limitation all DOCUMENTS that evidence or refute the legal and factual bases for such allegations and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent it calls for documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request insofar as the phrase "has an equivalent element, performs an equivalent step, or induces performance of an equivalent step" is vague and ambiguous and as such is not reasonably calculated to lead to the discovery of admissible evidence.

Wyeth also objects to this request as premature because under the Court's Scheduling Order initial expert reports are not due until September 28, 2007. Wyeth additionally objects to this request as premature in that discovery is still ongoing. In particular, Wyeth has not received complete discovery from Impax, and has not had

sufficient time to review and analyze the information contained therein. Full discovery from Impax, including expert discovery, is necessary to identify the full nature and scope of Impax's infringement. Moreover, because the claims have not been construed by the Court, the nature of Wyeth's infringement position may evolve depending on how Impax seeks to construe or apply the claims during the course of the litigation. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they are not protected by the attorney-client privilege and/or work product immunity, in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 91:

To the extent WYETH contends that there is a nexus between the commercial success of EFFEXOR XR or other EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE and the asserted claims in the PATENTS IN SUIT such that their commercial success is a secondary consideration of those claims' non-obviousness, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute those bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request as premature because fact discovery is just beginning and as being the subject of expert discovery. Under the Court's pretrial Scheduling Order, Wyeth's rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in

determining which documents are responsive to this request. Wyeth objects to this request to the extent it calls for documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 92:

To the extent WYETH contends that the following prior art does not anticipate the asserted claims of the PATENTS IN SUIT, DOCUMENTS CONCERNING all the legal and factual bases for WYETH's assertion that any limitation of the asserted claims is not disclosed in each of the following prior art, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to identify all PERSONS who have knowledge of these bases:

(a) EP 0 624 366, published 11/17/1994, "Controlled release formulation containing tramadol"

(b) U.S. Patent No. 6,440,457 B1, "Method of Administering Antidepressant Dosage Form"

(c) WO 94/27589, published 12/8/1994, "Antidepressant dosage form"

(d) AU 47732/90, published 7/12/90, "Sustained release pharmaceutical composition"

(e) WO 95/14460 published 6/1/1995, "Opioid formulations for treating pain"

(f) Troy *et al., J. Clin. Pharmacol.* 1995 (April) 35:404-409, "The pharmacokinetics of venlafaxine when given in a twice-daily regimen"

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contentions to Wyeth regarding any alleged anticipation of Wyeth's asserted claims.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 93:

To the extent WYETH contends that there was no motivation to combine two or more of the following prior art at the time of the asserted claims' date(s) of conception, DOCUMENTS CONCERNING all the legal and factual bases for such contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to identify all PERSONS who have knowledge of these bases:

(a) EP 0 624 366, published 11/17/1994, "Controlled release formulation containing tramadol"

(b) U.S. Patent No. 6,440,457 B1, "Method of Administering Antidepressant Dosage Form"

(c) WO 94/27589, published 12/8/1994, "Antidepressant dosage form"

(d) AU 47732/90, published 7/12/90, "Sustained release pharmaceutical composition"

(e) WO 95/14460 published 6/1/1995, "Opioid formulations for treating pain"

(f) Troy *et al., J. Clin. Pharmacol.* 1995 (April) 35:404-409, "The pharmacokinetics of venlafaxine when given in a twice-daily regimen"

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contentions to Wyeth regarding the manner in which any of the cited references allegedly provide motivation to combine two or more of the cited references or how any would allegedly render obvious any of the asserted claims.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 94:

DOCUMENTS CONCERNING the legal and factual bases WYETH relies on in its denials in paragraphs 1, 4-5, 7-36, 38, 40-47, 49-57 of WYETH'S REPLY, including without limitation DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases, what knowledge each PERSON has, and all DOCUMENTS that evidence these bases.

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 95:

To the extent WYETH contends that the statement:

The use of the one-a-day venlafaxine hydrochloride formulations of this invention reduces by adaptation, the level of nausea and incidence of emesis that attend the administration of multiple daily dosing.

from the PATENTS IN SUIT was not material to patentability and/or was not made to the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for Wyeth's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to identify all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contention to Wyeth regarding the quoted passage from the patents-in-suit.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 96:

To the extent WYETH contends that the statement:

> In clinical trials of venlafaxine hydrochloride ER, the probability of developing nausea in the course of the trials was greatly reduced after the first week.

from the PATENTS IN SUIT was not material to patentability and/or was not made to the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for Wyeth's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to identify all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contention to Wyeth regarding the quoted passage from the patents-in-suit.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 97:

To the extent WYETH contends that the statement:

> Venlafaxine ER showed a statistically significant improvement over conventional venlafaxine hydrochloride tablets in two eight-week and one 12 week clinical studies.

from the PATENTS IN SUIT was not material to patentability and/or was not made to the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contention to Wyeth regarding the quoted passage from the patents-in-suit.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-

client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 98:

To the extent WYETH contends that the statement:

> Thus, in accordance with this use aspect of the invention there is provided a method for reducing the level of nausea and incidence of emesis attending the administration of venlafaxine hydrochloride which comprises dosing a patient in need of treatment with venlafaxine hydrochloride with an extended release formulation of venlafaxine hydrochloride once a day in a therapeutically effective amount.

from the PATENTS IN SUIT was not material to patentability and/or was not made to the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it calls for documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its contention to Wyeth regarding the quoted passage from the patents-in-suit.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 99:

DOCUMENTS CONCERNING all the factual and legal bases for WYETH's statements in paragraphs 18, 19, and 21 of WYETH'S REPLY that "during the prosecution of the patents-in-suit, Wyeth never represented to the PTO that each clinical study, standing alone, established a statistically significant improvement of Effexor® XR over immediate release Effexor®," including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this document request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 100:

DOCUMENTS CONCERNING all the factual and legal bases for WYETH's denial of paragraph 68 of IMPAX's Counterclaims, as stated in paragraph 20 of WYETH'S REPLY, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 101:

To the extent WYETH contends that WYETH or the NAMED INVENTORS were not aware of an article by Lynn A. Cunningham, M.D., entitled *Once-Daily Venlafaxine Extended Release (XR) and Venlafaxine Immediate Release (IR) in Outpatients with Major Depression*, published in the volume 9, no. 3 of the Annals of Clinical Psychiatry in 1997 during the prosecution of the PATENTS IN SUIT, that this article was not material to patentability, and/or that this article was not withheld from the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege or immunity. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request.

Wyeth objects to this request to the extent it seeks information with respect to "WYETH" using Impax's definition of that term as being overly broad, unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence. This action involves Wyeth and not its past or present, U.S. or foreign subsidiaries, past or present, U.S. or foreign divisions, past or present, U.S. or foreign parent corporations, or "any related companies." In addition, Wyeth objects to Impax's definition of "Wyeth" to the extent these terms include former officers, directors, employees, agents, attorneys, and representatives as potentially including entities outside of Wyeth's possession, custody, or control, or calls for information that may be subject to confidentiality agreements and/or attorney-client privilege.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request as overly broad and irrelevant to any issue in the suit because Impax has not yet provided its unenforceability contentions to Wyeth with

respect to the Cunningham article despite its having been served with Wyeth Interrogatory No. 4 requesting Impax's unenforceability contentions in June 2006.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 102:

To the extent WYETH contends that, during the prosecution of the PATENTS IN SUIT, WYETH or the NAMED INVENTORS were not aware of ALZA's development of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE beyond the disclosure in publication WO 94/27589, that the information known about ALZA's development was not material to patentability, and/or that information known about ALZA's development was not withheld from the PTO with the intent to deceive, DOCUMENTS CONCERNING all the legal and factual bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request

as overly broad and irrelevant to any issue in the suit because Impax has not set forth allegations or contentions regarding "ALZA's development of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE."

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 103:

To the extent WYETH contends that the following passage:

> It was completely unexpected that an extended release formulation containing venlafaxine hydrochloride could be obtained because the hydrochloride of venlafaxine proved to be extremely water soluble.

from the PATENTS IN SUIT was not material to patentability and/or was not made to the PTO with the intent to deceive, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request as premature because under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007. Wyeth

further objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request as overly broad and irrelevant to any issues in the suit because Impax has not pled allegations or made contentions regarding the above quoted passage.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 104:

To the extent WYETH contends that analysis, study, test, trial, research, or experimental results prior to March 25, 1996 demonstrated that the EXTENDED RELEASE FORMULATION comprising VENLAFAXINE claimed in the PATENTS IN SUIT provided a therapeutic blood plasma concentration of VENLAFAXINE over a twenty four hour period with diminished incidences of nausea and emesis, DOCUMENTS sufficient to IDENTIFY such analysis, study, test, trial, research, or experimental results and DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it seeks "analysis, study, test, trial, research, or experimental results" as vague and ambiguous, overly broad, and unduly burdensome. Wyeth also objects to this request to the extent

it requires a legal conclusion in determining which documents are responsive to this request.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 105:

To the extent WYETH contends that analysis, study, test, trial, research, or experimental results prior to March 25, 1996 demonstrated that the EXTENDED RELEASE FORMULATION comprising VENLAFAXINE claimed in the PATENTS IN SUIT eliminated the troughs and peaks of drug concentration in a patient's blood plasma attending the therapeutic metabolism of plural daily doses of VENLAFAXINE, DOCUMENTS sufficient to IDENTIFY such analysis, study, test, trial, research, or experimental results and DOCUMENTS CONCERNING all the legal and factual bases for WYETH's contention, including without limitation all DOCUMENTS that evidence or refute these bases and DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases.

OBJECTION:

Wyeth objects to this request to the extent it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it seeks "analysis, study, test, trial, research, or experimental results" as vague and ambiguous, overly broad, and unduly burdensome. Wyeth also objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents to the extent they exist and are not protected by the attorney-client privilege and/or work product immunity.

IMPAX DOCUMENT REQUEST NO. 106:

All of WYETH's responses to Interrogatories and Requests for Admissions in the legal action *Alza Corp. v. Wyeth*, Case No. 06-CV-156, in the United States District Court for the Eastern District of Texas.

OBJECTION AND RESPONSE:

Wyeth objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of discovery responses from a different litigation involving a third party patent that is not the subject of this litigation. Impax has raised no specific contentions with respect to Alza nor has it provided any nexus between the relevance of the documents it seeks to any claim or defense in this case. Wyeth further objects to this request to the extent it seeks documents and things subject to the rights of third parties not affiliated with Wyeth. Further, to the extent information is designated as confidential by a third party, it would be unduly burdensome to attempt to redact this information. In addition, Wyeth objects to the production of non-Wyeth information subject to a protective order entered in a litigation other than the above-captioned Impax litigation.

IMPAX DOCUMENT REQUEST NO. 107:

All DOCUMENTS CONCERNING any analysis of infringement, non-infringement, validity, invalidity, enforceability, or unenforceability of any of U.S. Patent No. 6,440,457 B1 or the PATENTS IN SUIT, including without limitation any expert report, conducted by, or on behalf of, or at the request of WYETH, in the legal action *Alza Corp. v. Wyeth*, Case No. 06-CV-156, in the United States District Court for the Eastern District of Texas.

OBJECTION AND RESPONSE:

Wyeth objects to this request to the extent it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit, and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of documents concerning a different litigation involving a third party patent that is not the subject of this litigation. Wyeth further objects to this request to the extent it seeks documents and things subject to the rights of third parties not affiliated with Wyeth. Further, to the extent information is designated as confidential by a third party, it would be unduly burdensome to attempt to redact this information. In addition, Wyeth objects to the production of non-Wyeth information subject to a protective order entered in a litigation other than the above-captioned Impax litigation.

IMPAX DOCUMENT REQUEST NO. 108:

All transcripts of deposition of WYETH's witnesses in the legal action *Alza Corp. v. Wyeth*, Case No. 06-CV-156, in the United States District Court for the Eastern District of Texas.

OBJECTION AND RESPONSE:

Wyeth objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of deposition transcripts concerning a different litigation involving a third party patent that is not the subject of this litigation. Wyeth further objects to this request to the extent it seeks documents and things subject to the rights of third parties not affiliated with Wyeth. Further, to the extent information is designated as confidential by a third party, it would be unduly burdensome to attempt to redact this information. In addition, Wyeth objects to the production of non-Wyeth information subject to a protective order entered in a litigation other than the above-captioned Impax litigation.

IMPAX DOCUMENT REQUEST NO. 109:

All publications, including without limitation, U.S. and foreign patents, textbooks, articles, conference proceedings, treatises, theses, tutorials, speeches, and presentations, disclosing all or part of the limitations set forth in the claim(s) of any of U.S. Patent No. 6,440,457 B1 or the PATENTS IN SUIT, dated or in existence before March 25, 1996, produced by any party in the legal action *Alza Corp. v. Wyeth*, Case No. 06-CV-156, in the United States District Court for the Eastern District of Texas.

OBJECTION AND RESPONSE:

Wyeth objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of documents concerning a different litigation involving a third party patent that is not the subject of this litigation. Wyeth also objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to the request. To the extent this request

does not require a legal conclusion in determining which documents are responsive to the request, Wyeth objects to this request as overly broad and unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence in seeking all publications dated or in existence before March 31, 1996.

IMPAX DOCUMENT REQUEST NO. 110:

All DOCUMENTS CONCERNING claim construction(s) proposed by WYETH in the legal action *Alza Corp. v. Wyeth*, Case No. 06-CV-156, in the United States District Court for the Eastern District of Texas.

OBJECTION AND RESPONSE:

Wyeth objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of documents concerning a different litigation involving a third party patent that is not the subject of this litigation. Wyeth also objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to this request. Wyeth further objects to this request to the extent it seeks documents and things subject to the rights of third parties not affiliated with Wyeth. Further, to the extent information is designated as confidential by a third party, it would be unduly burdensome to attempt to redact this information. In addition, Wyeth objects to the production of non-Wyeth information subject to a protective order entered in a litigation other than the above-captioned Impax litigation. Wyeth further objects to this request to the extent it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of

litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

IMPAX DOCUMENT REQUEST NO. 111:

All publications, including without limitation, U.S. and foreign patents, textbooks, articles, conference proceedings, treatises, theses, tutorials, speeches, and presentations, disclosing all or part of the limitations set forth in the claim(s) of the PATENT IN SUIT, dated or in existence before March 25, 1996, produced by any party in the legal action *Wyeth v. Anchen Pharmaceuticals, Inc.*, Case No. 06-CV-386, in the United States District Court in the Central District of California.

OBJECTION:

Wyeth objects to this request to the extent it requires a legal conclusion in determining which documents are responsive to the request. To the extent this request does not require a legal conclusion in determining which documents are responsive to the request, Wyeth objects to this request as overly broad, unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence in seeking all publications dated or in existence prior to March 26, 1996.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce the requested documents.

IMPAX DOCUMENT REQUEST NO. 112:

All DOCUMENTS CONCERNING claim construction(s) proposed by WYETH in the legal action *Wyeth v. Anchen Pharmaceuticals, Inc.*, Case No. 06-CV-386, in the United States District Court in the Central District of California.

OBJECTION:

Wyeth objects to this request to the extent it seeks documents subject to the rights of third parties not affiliated with Wyeth. In addition, Wyeth objects to the production of non-Wyeth documents or information subject to a protective order entered in a litigation other than the above-captioned litigation. Wyeth further objects to this request as unduly burdensome, overly broad, irrelevant to any issue in this suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks the production of pleadings and other documents, including but not limited to, the deposition transcripts of Anchen witnesses, expert reports or expert depositions, and/or hearing transcripts, concerning infringement of products other than those at issue in this litigation. The Anchen litigation involves a different party and product, and information regarding that Party and product is simply not relevant to this present litigation. Furthermore, Anchen is likely to designate the bulk of this information as confidential and subject to the protective order in place in the Anchen litigation, and it would be unduly burdensome to attempt to redact this information. Moreover, Anchen, not Wyeth, would have to redact information it designated as confidential. In addition, Wyeth objects to this request to the extent it seeks documents protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or is otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce all non-privileged documents produced by Wyeth in response to document requests in the

Anchen litigation. Furthermore, Wyeth will produce Markman briefings and portions of expert reports, expert depositions and contention interrogatory answers concerning claim construction in the Anchen litigation once Anchen has redacted its confidential information or given Wyeth permission to produce it.

IMPAX DOCUMENT REQUEST NO. 113:

All DOCUMENTS CONCERNING any analysis of validity, invalidity, enforceability, or unenforceability of any of the PATENTS IN SUIT, including without limitation any expert report, conducted by, or on behalf of, or at the request of WYETH, in the legal action *Wyeth v. Anchen Pharmaceuticals, Inc.*, Case No. 06-CV-386, in the United States District Court in the Central District of California.

OBJECTION:

Wyeth objects to this request to the extent it seeks documents subject to the rights of third parties not affiliated with Wyeth. In addition, Wyeth objects to the production of non-Wyeth documents or information subject to a protective order entered in a litigation other than the above-captioned litigation. Wyeth further objects to this request to the extent it seeks documents that are protected by the attorney-client privilege, prepared or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce portions of Wyeth's expert reports, Wyeth's expert depositions and Wyeth's contention interrogatory answers concerning validity and enforceability in the Anchen litigation once Anchen has redacted its confidential information or given Wyeth permission to produce it.

IMPAX DOCUMENT REQUEST NO. 114:

All DOCUMENTS CONCERNING propranolol, dated or in existence before July 16, 2002, provided to WYETH by Imperial Chemical Industry PLC, a.k.a. ICI, or its affiliates or subsidiaries known to WYETH, including without limitation DOCUMENTS CONCERNING manufacture of EXTENDED RELEASE FORMULATIONS comprising propranolol.

OBJECTION:

Wyeth objects to this document request as overly broad, unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence to the extent it seeks "[a]ll DOCUMENTS CONCERNING propranol" "provided to WYETH." Wyeth objects to this request to the extent it seeks documents subject to the rights of third parties, including Imperial Chemical Industry, PLC., not affiliated with Wyeth.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce non-privileged documents collected in 2004 and produced in the Teva litigation (1) pertaining to Inderal® LA contained in the personal files of the inventors of the patents-in-suit and (2) non-privileged documents located in the archived Rouses Point Pharmaceutical Sciences department administrative chronological files (the department files for the department in which the inventors worked) pertaining to Inderal® LA that were authored or received by any of the inventors of the patents-in-suit.

IMPAX DOCUMENT REQUEST NO. 115:

All DOCUMENTS CONCERNING the article by Lynn A. Cunningham, M.D., entitled *Once-Daily* Venlafaxine *Extended Release (XR) and Venlafaxine Immediate Release (IR) in Outpatients with Major Depression*, published in the volume 9, no. 3 of the Annals of Clinical Psychiatry in 1997.

OBJECTION:

Wyeth objects to this request as overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence to the extent it calls for "[a]ll DOCUMENTS CONCERNING" the Cunningham article. For example, Wyeth objects to the production of information such as voluminous raw data and data compilations from clinical trials, manufacturing, production, quality control, quality assurance and documents containing patient identifying information that would raise privacy issues.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 116:

All DOCUMENTS CONCERNING the article by Richard Entsuah, Ph.D. and Rohini Chitra, entitled *A benefit-risk analysis of once-daily venlafaxine extended release (XR) and venlafaxine immediate release (IR) in outpatients with major depression*, published in volume 33, no. 4 of Psychopharmacology Bulletin in 1997.

OBJECTION:

Wyeth objects to this request as overly broad, unduly burdensome and not reasonably calculated to lead to the discovery of admissible evidence to the extent it calls for "[a]ll DOCUMENTS CONCERNING" the Entsuah and Chitra article. For example, Wyeth objects to the production of information such as voluminous raw data and data compilations from clinical trials, manufacturing, production, quality control, quality assurance and documents containing patient identifying information that would raise privacy issues.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 117:

DOCUMENTS CONCERNING all studies, tests, trials, research, or experiments conducted that compare incidences of nausea and emesis between patients receiving EFFEXOR and patients receiving EFFEXOR XR or any WYETH EXTENDED RELEASE FORMULATION comprising VENLAFAXINE, including without limitation all DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of such studies, tests, trials, research, or experiments, what knowledge each PERSON has, and all DOCUMENTS that evidence or refute such studies, tests, trials, research, or experiments.

OBJECTION:

Wyeth objects to this request as overly broad, unduly burdensome, vague and ambiguous, and not reasonably calculated to lead to the discovery of admissible evidence to the extent it calls for "DOCUMENTS CONCERNING all studies, tests, trials,

research, or experiments conducted." For example, Wyeth objects to the production of information such as voluminous raw data and data compilations from clinical trials, manufacturing, production, quality control, quality assurance and documents containing patient identifying information that would raise privacy issues. Wyeth also objects to this document request to the extent it uses the phrase "studies, tests, trials, research, or experiments" as vague and ambiguous, overly broad and unduly burdensome and will construe the phrase as referring to only pharmacokinetic and clinical trials. Wyeth also objects to this request to the extent it seeks documents concerning any "WYETH EXTENDED RELEASE FORMULATION comprising VENLAFAXINE" which was developed after the effective filing date of the patents in suit, other than Effexor® XR, as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information. Wyeth further objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log. In addition, documents identified in Wyeth's response to Impax Interrogatory No. 29 have been produced.

IMPAX DOCUMENT REQUEST NO. 118:

DOCUMENTS CONCERNING any and all statistical analyses conducted by, or on behalf of, or at the request of, in the custody or possession of WYETH, that compare nausea and emesis between patients receiving EFFEXOR and patients receiving EFFEXOR XR or any WYETH EXTENDED RELEASE FORMULATION comprising venlafaxine.

OBJECTION:

Wyeth objects to this request to the extent that it calls for information that is protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or is otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it seeks documents concerning any "WYETH EXTENDED RELEASE FORMULATION comprising VENLAFAXINE" which was developed after the effective filing date of the patents in suit, other than Effexor® XR, as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information. Wyeth further objects to this Interrogatory as overly broad, unduly burdensome, and not reasonably calculated to lead to the discovery of admissible evidence to the extent the Interrogatory calls for information "in the custody or possession" of "Wyeth", as that term is defined by Impax for the reasons set forth in Wyeth's General Objection No. 12, above.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a

withheld document log. In addition, the March 11, 2005 Memorandum of Gary Carmon and Addendum (WYETH318-008547-8591); the expert reports of Dr. Ronald Thisted (produced in this litigation at production numbers WYETH318-004115-4256); the expert reports of Dr. Eric Hollander (produced in this litigation at production numbers WYETH318-003984-04055); the expert reports of Dr. Ronald Sawchuk (produced in this litigation at production numbers WYETH318-003584-3780); and the deposition transcripts of Lawrence Alaburda and Richard Mangano (produced in this litigation at production numbers WYETH300-000001-302 and WYETH300-000969-1279) have been produced.

IMPAX DOCUMENT REQUEST NO. 119:

DOCUMENTS CONCERNING all relationships, agreements, pacts, engagements, or understandings between WYETH and ALZA CONCERNING ALZA's research and development of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE, dated or in existence before July 16, 2002, including without limitation DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these relationships, agreements, pacts, engagements, or understandings what knowledge each PERSON has, and all DOCUMENTS that evidence these relationships, agreements, pacts, engagements, or understandings, or inquiries.

OBJECTION:

Wyeth objects to this request as overly broad, unduly burdensome, vague and ambiguous, irrelevant, and not reasonably calculated to lead to the discovery of admissible evidence insofar as Impax has not articulated any nexus between the information sought and any claim or defense in this litigation. Wyeth further objects to this request to the extent it seeks documents concerning any "relationships, agreements, pacts, engagements, or understandings or inquiries" as vague and

ambiguous. Wyeth further objects to this request to the extent that it calls for information that is protected by the attorney-client privilege, prepared, or obtained in anticipation of litigation or for trial, or is otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity. Wyeth further objects to this request to the extent it encompasses extended release venlafaxine formulation projects not begun until after the effective filing date of the patents in suit as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 120:

All DOCUMENTS CONCERNING ALZA's research and development of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE, including without limitation DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of such research and development, what knowledge each PERSON has, and all DOCUMENTS that evidence or refute such research and development.

OBJECTION:

Wyeth objects to this request to the extent it calls for the production of documents outside of the possession or control of Wyeth. Wyeth also objects to this

request to the extent it calls for production of third party documents subject to a protective order in third party litigation.

Wyeth further objects to this request to the extent it encompasses extended release venlafaxine formulation projects not begun until after the effective filing date of the patents in suit as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 121:

All DOCUMENTS CONCERNING WYETH's development of EXTENDED RELEASE FORMULATION comprising VENLAFAXINE, including without limitation DOCUMENTS CONCERNING WYETH's efforts to develop Hydrogel tablets, Gelucire capsules or coated spheroids.

OBJECTION:

Wyeth objects to this request as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence, and unreasonably cumulative and duplicative to the extent the request seeks documents from the multitude of Plaintiff's employees involved in, for example, routine testing, scale up, maintenances, purchasing or qualification of raw materials and equipment, manufacturing, packaging, etc. Wyeth also objects to the production of

voluminous raw data gathered from, for example, *in vitro* studies, preclinical studies, clinical trials, production runs, quality control procedures, and routine testing as unduly burdensome and unreasonably cumulative and duplicative. Wyeth further objects to this request to the extent it seeks documents concerning any venlafaxine-containing extended release formulation developed after the effective filing date of the patents-in-suit other than EFFEXOR® XR, as overly broad, unduly burdensome, irrelevant to any issue in the suit, not reasonably calculated to lead to the discovery of admissible evidence and as seeking highly sensitive future product information.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce documents and things previously produced by Wyeth in response to document requests in the Teva litigation and will identify protected documents associated with that production on a withheld document log.

IMPAX DOCUMENT REQUEST NO. 122:

To the extent WYETH contends that the asserted claims of the PATENTS IN SUIT are not obvious in view of WYETH's Inderal® LA (propranolol HCl) Long-Acting Capsules, DOCUMENTS CONCERNING all the factual and legal bases for WYETH's contention, including without limitation DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of these bases, what knowledge each person has, and all DOCUMENTS that evidence or refute these bases.

OBJECTION:

Wyeth objects to this request to the extent that it seeks documents that are protected by the attorney-client privilege, prepared, or obtained in anticipation of

litigation or for trial, or are otherwise subject to the work product doctrine or any other applicable rights, privilege, or immunity.

Wyeth further objects to this request to the extent it requires a legal conclusion to determine whether documents are responsive to this request. Wyeth further objects to this request as premature in that under the Court's Scheduling Order, rebuttal expert reports are not due until October 31, 2007.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce non-privileged documents responsive to this request in accordance with the Court's Scheduling Order.

IMPAX DOCUMENT REQUEST NO. 123:

DOCUMENTS CONCERNING all studies, tests, trials, research, or experiments WYETH conducted prior to July 16, 2002 that compare chemical properties, including without limitation solubility, of propranolol and its salts with that of VENLAFAXINE and its salts, including without limitation DOCUMENTS sufficient to IDENTIFY all PERSONS who have knowledge of such studies, tests, trials, research, or experiments, what knowledge each PERSON has, and all DOCUMENTS that evidence or refute such studies, tests, trials, research, or experiments.

OBJECTION:

Wyeth objects to this request to the extent it seeks "DOCUMENTS CONCERNING all studies, tests, trials, research, or experiments WYETH conducted prior to July 16, 2002 that compare chemical properties" of propranolol and venlafaxine as overly broad, unduly burdensome, and irrelevant to any issue in the suit to the extent it seeks information regarding documents not authored or received by the inventors of the patents-in-suit. Wyeth further objects to this request to the extent it seeks

information regarding "studies, tests, trials, research, or experiments, that compare chemical properties" of venlafaxine and propranolol as vague and ambiguous, overly broad and unduly burdensome.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce non-privileged documents collected in 2004 pertaining to Inderal® LA contained in the personal files of the inventors of the patents-in-suit and non-privileged documents located in the archived Rouses Point Pharmaceutical Sciences department administrative chronological files (the department files for the department in which the inventors worked) pertaining to Inderal® LA that were authored or received by any of the inventors of the patents-in-suit.

IMPAX DOCUMENT REQUEST NO. 124:

All DOCUMENTS CONCERNING EXTENDED RELEASE FORMULATIONS comprising propranolol developed or manufactured by Inglewood Laboratories or Elan Corporation, PLC, dated or in existence before July 16, 2002.

OBJECTION:

Wyeth objects to this request to the extent it seeks documents concerning extended release formulations comprising propranolol not authored or received by the inventors of the patents-in-suit as overly broad, unduly burdensome, irrelevant to any issue in the suit and not reasonably calculated to lead to the discovery of admissible evidence. Wyeth further objects to this request to the extent it seeks documents subject to the rights of third parties.

RESPONSE:

Subject to the General and Specific Objections, Wyeth will produce non-privileged documents collected in 2004 pertaining to Inderal® LA contained in the personal files of the inventors of the patents-in-suit and non-privileged documents located in the archived Rouses Point Pharmaceutical Sciences department administrative chronological files (the department files for the department in which the inventors worked) pertaining to Inderal® LA that were authored or received by any of the inventors of the patents-in-suit.

Dated: October 10, 2006

By:

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EXHIBIT 6

OAO 88 (Rev. 1/94) Subpoena in a Civil Case

Issued by the

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

WYETH
V.
IMPAX LABORATORIES, INC.

SUBPOENA IN A CIVIL CASE

Case Number:[1] Civil Action No. 06-222 JJF in the U.S. District Court for the District of Delaware

TO: ALZA CORPORATION, 1900 Charleston Road, Mountain View, CA 94043

☐ YOU ARE COMMANDED to appear in the United States District court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☐ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION	DATE AND TIME

☒ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects): See Attachment A

PLACE	DATE AND TIME
Heller Ehrman LLP, 333 Bush St., San Francisco, CA 94104-2878	December 21, 2006

☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. ~~Federal Rules~~ of Civil Procedure, 30(b)(6).

ISSUING OFFICER'S SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
	November 21, 2006

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER
Samuel F. Ernst, attorney for Defendant Impax Laboratories, Inc., Heller Ehrman LLP, 333 Bush St., San Francisco, CA 94104-2878

(See Rule 45, Federal Rules of Civil Procedure, Parts C & D on next page)

[1]If action is pending in district other than district of issuance, state district under case number.

AO 88 (Rev 1/94) Subpoena in a Civil Case

PROOF OF SERVICE

DATE SERVED:	PLACE
SERVED ON (PRINT NAME)	MANNER OF SERVICE
SERVED BY (PRINT NAME)	TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____

SIGNATURE OF SERVER

ADDRESS OF SERVER

Rule 45, Federal Rules of Civil Procedure, Parts C & D:

(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction which may include, but is not limited to, lost earnings and reasonable attorney's fee.

(2) (A) A person commanded to produce and permit inspection and copying of designated books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(B) Subject to paragraph (d) (2) of this rule, a person commanded to produce and permit inspection and copying may, within 14 days after service of subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to inspection or copying of any or all of the designated materials or of the premises. If objection is made, the party serving the subpoena shall not be entitled to inspect and copy materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production. Such an order to comply production shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection and copying commanded.

(3) (A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance,

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to the provisions of clause (c) (3) (B) (iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held, or

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies, or

(iv) subjects a person to undue burden.

(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena, or, if the party in who behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

(d) DUTIES IN RESPONDING TO SUBPOENA.

(1) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(2) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

ATTACHMENT A

DEFINITIONS

For the purpose of this subpoena, the following words and phrases are defined as follows:

1. "ALZA" means Alza Corporation, and its past or present directors, officers, employees, agents, representatives or attorneys.

2. "WYETH" means the corporation known as Wyeth and that company as it was previously named (including, for example, American Home Products) and any related companies, parents, divisions, or subsidiaries, past or present (including, for example, Wyeth Ayerst Laboratories), located in the U.S. or abroad, and the past or present directors, officers, employees, agents, representatives or attorneys thereof.

3. "EXTENDED RELEASE FORMULATION" means a formulation which releases the active ingredient at a slower rate than would an immediate release formulation of said active ingredient such that the desired dosing frequency is or would be less than that for the immediate release formulation.

4. "VENLAFAXINE" means the compound 1-[(2-dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol commonly known as venlafaxine, as well as all compositions, formulations, and preparations containing venlafaxine, including without limitation VENLAFAXINE and other pharmaceutically acceptable salts of venlafaxine.

5. "OROS®" means ALZA's drug delivery technology known as OROS® osmotic technology, including all present and past formulations of same.

6. "CONCERNING" means referring to, relating to, regarding, reflecting, associated with, comprising, constituting, containing, demonstrating, describing, discussing, evidencing, evincing, indicating, on the subject of, on the topic of, showing, or prepared in connection with the stated matter.

7. "DOCUMENT" or "DOCUMENTS" means all written, printed, typed, electronically produced, electronically stored, photostatic, photographed, recorded, or otherwise reproduced communications or records of every kind and description, whether comprised of letters, words, pictures, sounds, symbols, or combinations thereof. DOCUMENTS include originals as well as drafts, copies, marked-up copies, non-identical duplicates, and computer files, including backup or archival copies.

8. "COMMUNICATION" means any contact between two or more persons, including but not limited to oral or written contact, in person or via e-mail, telephone, letters, video or audio recording, discussions, or other contact.

9. "THE LITIGATION" refers to the litigation captioned *Wyeth v. Impax Laboratories, Inc.*, Civil Action No. 06-222(JFF) in the U.S. District Court for the District of Delaware.

INSTRUCTIONS

1. All documents should be produced in a form that renders them susceptible to copying.

2. Each document should be segregated and identified by the request to which it is primarily responsive or produced as it is kept in the usual course of business.

3. If ALZA is unable to comply fully with any request herein, please comply to the extent possible and provide a detailed explanation as to why full compliance is not possible.

4. All requests herein are directed to those documents within ALZA's possession, custody or control, or within the possession, custody or control of ALZA's agents, servants, employees, and attorneys. They also are directed to those firms, corporations, partnerships, or trusts that ALZA controls and to documents in the possession, custody or control of employees, agents and representatives of such entities.

5. Documents may be produced bearing a designation that they are confidential. Such documents shall be maintained in confidence and for outside counsel's eyes only according to Rule 26.2 of Local Rules of Civil Practice and Procedure for the United States District Court for the District of Delaware until the entry of a protective order in THE LITIGATION. All documents produced in response to this subpoena shall be used only for the purpose of THE LITIGATION.

6. If any document called for is withheld under a claim of privilege of protection against discovery, please give the following information for that document:

   - The name and title of the author(s);
   - The name and title of each person to whom the document was addressed;
   - The name and title of each person to whom a copy of the document was sent, directed, circulated, or distributed;
   - The date of the document;
   - A brief description of the nature and subject matter of the document in sufficient detail to permit assessment of the applicability of the asserted privilege or immunity;

- The basis of the claim, privilege or protection against discovery;

REQUESTS FOR DOCUMENTS AND THINGS

1. Research and development DOCUMENTS, created prior to November 5, 1997, CONCERNING ALZA's research and development (including joint research and development with WYETH) of EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE or VENLAFAXINE formulations utilizing OROS® sufficient to show the following:

   a) the composition of said formulations;

   b) the in vitro dissolution profile of said formulations;

   c) the pharmacokinetics of said formulations, including blood plasma levels as a function of time, the peak blood plasma level of venlafaxine hydrochloride (C_{max}) provided by said formulations and the time to peak blood plasma level of venlafaxine hydrochloride (t_{max}) provided by said formulations;

   d) the number of hours over which said formulations achieved a therapeutically effective blood plasma level of venlafaxine hydrochloride;

   e) the incidence of nausea caused by such formulations as compared to immediate release formulations;

   f) the incidence of emesis caused by such formulations as compared to immediate release formulations

2. All COMMUNICATIONS between ALZA and WYETH prior to November 5, 1997 concerning the research and development (including joint research and development with WYETH) of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE or a VENLAFAXINE formulation utilizing OROS®.

3. DOCUMENTS sufficient to show a summary or report of *in vivo* and *in vitro* test results, performed prior to November 5, 1997, CONCERNING ALZA's research and development (including joint research and development with WYETH) of EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE or VENLAFAXINE formulations utilizing OROS®.

4. Samples of each EXTENDED RELEASE FORMULATION comprising a VENLAFAXINE formulation utilizing OROS® developed by ALZA (including as part of a joint research and development effort with WYETH) prior to November 5, 1997.

EXHIBIT 7

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA

WYETH, Plaintiff, v. IMPAX LABORATORIES, INC., Defendant.	)	Case No. 1:06-cv-00222-JJF Pending in the United States District Court for the District of Delaware

ALZA CORPORATION'S OBJECTIONS AND RESPONSES TO SUBPOENA DUCES TECUM FROM IMPAX LABORATORIES, INC.

Alza Corporation ("Alza") hereby responds to the subpoena served on Alza by Impax Laboratories, Inc. ("Impax") on November 21, 2006.

GENERAL OBJECTIONS

Alza makes the following general objections to the subpoena. To the extent applicable, each general objection is part of each objection and/or response to each document request contained in Attachment A of the subpoena and to each of Impax's instructions and definitions. Without regard to the objections made in these General Objections, Alza reserves the right to make any appropriate objections at any deposition, hearing or trial of this matter. Moreover, Alza's responses are within the scope of Alza's reasonable investigation at this time and Alza reserves the right to amend and/or supplement its responses, objections and/or production of documents as appropriate.

1. Alza objects to the direction in the subpoena to produce and permit inspection and copying of the requested documents on December 21, 2006, in San Francisco, CA, as unreasonable and unduly burdensome. Alza will undertake reasonable efforts to produce the

requested documents at the office of its counsel, Jenner & Block LLP, 330 North Wabash Avenue, Chicago, Illinois 60611, subject to Alza's objections, beginning on December 21, 2006, or as soon thereafter as an appropriate protective order is in place and continuing thereafter until completion.

2. Alza objects to the definitions, instructions and document requests to the extent that they seek DOCUMENTS that are protected by the attorney-client privilege, the attorney work product doctrine, or that are otherwise not subject to discovery by virtue of Rule 26(b)(3) of the Federal Rules of Civil Procedure or any other privilege or doctrine recognized by law.

3. Alza objects to the definitions, instructions and document requests to the extent they seek to impose greater burdens on Alza than those required by the Federal Rules of Civil Procedure or the Local Rules of the United States District Court for the Northern District of California. Alza responds to this subpoena in accordance with its obligations under the Federal Rules of Civil Procedure and the Local Rules of the United States District Court for the Northern District of California.

4. Alza objects to the definitions, instructions and document requests to the extent they seek documents or information not within Alza's possession, custody or control.

5. Alza objects to the definitions, instructions and document requests to the extent they seek documents or information that are cumulative, duplicative or already known or available to Impax.

6. Alza objects to the definition of "ALZA" as vague, ambiguous, overbroad and unduly burdensome including, without limitation, to the extent it is intended to include past "directors, officers, employees, agents, representatives or attorneys" no longer within the control of Alza.

7. Alza objects to the definition of "WYETH" to the extent that it is vague, ambiguous and overbroad including, without limitation, to the extent that it purportedly includes but does not define "any related companies."

8. Alza objects to the definition of "EXTENDED RELEASE FORMULATION" as vague and ambiguous.

9. Alza objects to the definition of "OROS®" as vague and ambiguous.

10. Alza objects to the definitions of "CONCERNING", "DOCUMENT", "DOCUMENTS", and "COMMUNICATION" to the extent that the definitions seek to impose a greater burden on Alza than those required by the Federal Rules of Civil Procedure or the Local Rules of the United States District Court for the Northern District of California.

11. Alza objects to the production of documents that are confidential and will produce such documents only after an appropriate protective order is in place that, *inter alia*, limits the use of any documents produced to use in connection with THE LITIGATION and limits the distribution of and access to information contained in such produced documents to current outside counsel for Wyeth and Impax, namely, Morris, Nichols, Arsht & Tunnell; Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.; Morris, James, Hitchens & Williams; and Heller Ehrman LLP.

12. Alza objects to the production of documents that are subject to a contractual obligation of confidentiality to Wyeth and will produce such documents only after an appropriate agreement from Wyeth that allows production of such documents.

13. Alza objects to undertaking a search of archive backup tapes of electronic mail as unreasonable, overbroad and unduly burdensome and Alza has not undertaken such a search.

14. Alza's objections and responses are the result of Alza's reasonable efforts to respond in good faith to the subpoena's document requests as Alza understands and interprets them. Alza reserves the right to supplement its objections and responses to these requests if Impax asserts an interpretation different from the interpretation of Alza.

REQUEST FOR DOCUMENTS AND THINGS

REQUEST NO. 1:

Research and development DOCUMENTS, created prior to November 5, 1997, CONCERNING ALZA'S research and development (including joint research and development with WYETH) of EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE or VENLAFAXINE formulations utilizing OROS® sufficient to show the following:

a. the composition of said formulations;

b. the in vitro dissolution profile of said formulations;

c. the pharmacokinetics of said formulations, including blood plasma levels as a function of time, the peak blood plasma level of venlafaxine hydrochloride (C_{max}) provided by said formulations and the time to peak blood plasma level of venlafaxine hydrochloride (t_{max}) provided by said formulations;

d. the number of hours over which said formulations achieved a therapeutically effective blood plasma level of venlafaxine hydrochloride;

e. the incidence of nausea caused by such formulations as compared to immediate release formulations;

f. the incidence of emesis caused by such formulations as compared to immediate release formulations;

g. the incidence of emesis caused by such formulations as compared to immediate release formulations.

RESPONSE TO REQUEST NO. 1:

Alza reincorporates all of its General Objections as if specifically alleged herein. Alza specifically objects to this request as vague, ambiguous and overbroad.

Without waiving these objections and subject thereto, Alza responds as follows: Alza will provide documents it has been able to locate that are reasonably responsive to Alza's understanding of this request once an appropriate protective order is in place.

REQUEST NO. 2:

All COMMUNICATIONS between ALZA and WYETH prior to November 5, 1997 concerning the research and development (including joint research and development with WYETH) of an EXTENDED RELEASE FORMULATION comprising VENLAFAXINE or a VENLAFAXINE formulation utilizing OROS®.

RESPONSE TO REQUEST NO. 2:

Alza reincorporates all of its General Objections as if specifically alleged herein.

Without waiving these objections and subject thereto, Alza responds as follows: Alza will provide documents it has been able to locate that are reasonably responsive to Alza's understanding of this request once an appropriate protective order is in place.

REQUEST NO. 3:

DOCUMENTS sufficient to show a summary or report of *in vivo* and *in vitro* test results, performed prior to November 5, 1997, CONCERNING ALZA'S research and development (including joint research and development with WYETH) of EXTENDED RELEASE FORMULATIONS comprising VENLAFAXINE or VENLAFAXINE formulations utilizing OROS®.

RESPONSE TO REQUEST NO. 3:

Alza reincorporates all of its General Objections as if specifically alleged herein.

Without waiving these objections and subject thereto, Alza responds as follows: Alza will provide documents it has been able to locate that are reasonably responsive to Alza's understanding of this request once an appropriate protective order is in place.

REQUEST NO. 4:

Samples of each EXTENDED RELEASE FORMULATION comprising a VENLAFAXINE formulation utilizing OROS® developed by ALZA (including as part of a joint research and development effort with WYETH) prior to November 5, 1997.

RESPONSE TO REQUEST NO. 4:

Alza reincorporates all of its General Objections as if specifically alleged herein.

Without waiving these objections and subject thereto, Alza responds as follows: Alza has not located any such samples after a reasonable search.

Date: December 21, 2006

By: _____

Harry J. Roper
Steven R. Trybus
JENNER & BLOCK LLP
330 N. Wabash
Chicago, IL 60611-7603
(312) 222-9350

Attorneys for Alza Corporation

CERTIFICATE OF SERVICE

I hereby certify that, on December 21, 2006, true and correct copies of the foregoing **ALZA CORPORATION'S OBJECTIONS AND RESPONSES TO SUBPOENA DUCES TECUM FROM IMPAX LABORATORIES, INC.**, were caused to be served upon counsel for Wyeth and Impax Laboratories, Inc., in the manner indicated below:

VIA FIRST CLASS MAIL

WYETH'S COUNSEL

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Melissa Stone Meyers
Karen Jacobs Louden
Morris, Nichols, Arsht & Tunnell
1201 North Market Street
P.O. Box 1347
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Basil J. Lewris
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Finnegan, Henderson, Farabow, Garrett & Dunner L.L.P.
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333 Bush Street
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John M. Benassi
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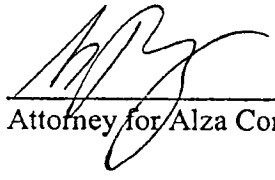

Attorney for Alza Corporation

EXHIBIT 8

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH,	)	
Plaintiff,	)	Civil Action No.: 06-222 (JJF)
v.	)	
IMPAX LABORATORIES, INC.,	)	
Defendant.	)	

STIPULATED PROTECTIVE ORDER REGARDING THE PRODUCTION OF DOCUMENTS BY ALZA CORPORATION IN RESPONSE TO SUBPOENA

WHEREAS, Defendant Impax Pharmaceuticals served on third party Alza Corporation ("Alza") a subpoena issued by the District Court for the Northern District of California, ("the Subpoena"), requesting the production of certain documents and information for use in the above-styled proceeding (the "Proceeding"), many of which contain trade secrets, or other confidential and proprietary, scientific, technical, financial, strategic, business planning, business arrangement, competitive, research, development, or other kinds of commercially sensitive information within the meaning of Federal Rule of Civil Procedure 26(c)(7);

WHEREAS, Alza and the parties, through their respective counsel, have agreed that a Stipulated Protective Order preserving the confidentiality of certain documents and information produced in response to the Subpoena should be entered by the United States District Court for the District of Delaware; and

WHEREAS, the parties have established good cause for entry of this Stipulated Protective Order;

IT IS HEREBY STIPULATED AND AGREED, SUBJECT TO THE APPROVAL AND ORDER OF THE COURT THAT:

1. Alza may designate as "Highly Confidential" all or any part of any discovery and other materials produced in response to the Subpoena that contain sensitive financial, patent, trademark, copyright, trade secret, marketing, customer, research, manufacture, regulatory, commercial, business, strategic, or product development information, or any other confidential technical or non-technical information or know-how of such a nature as to be protectable under Federal Rule of Civil Procedure 26(c)(7).

2. Material designated by Alza as Highly Confidential information, including all information derived therefrom, and all copies, summaries, abstracts, excerpts, indices, and descriptions of such material shall be held in confidence by the receiving party, shall be used only by persons permitted access to it under this Protective Order, and shall not be used for any purpose other than in connection with this litigation or appeal of this proceeding. Material designated by Alza as Highly Confidential information shall not be used for any research, development, manufacture, patent filing or prosecution, financial purpose, commercial purpose, marketing purpose, business purpose, regulatory purpose, Citizen's Petitions, lawsuits against the FDA, or any other litigation, regulatory or administrative proceeding, mediation or arbitration.

Designation Procedure

3. Designation by Alza of a document or thing as Highly Confidential information shall be made by stamping it with the legend "HIGHLY CONFIDENTIAL" or "HIGHLY CONFIDENTIAL SUBJECT TO PROTECTIVE ORDER" as reasonably appropriate when it is produced. Anything that cannot be so marked on its face shall be marked by placing the appropriate legend on a container or package in which the thing is produced or on a tag attached

thereto. Each page of each document and each thing produced in response to the Subpoena shall bear an identifying number.

Documents and things produced by Alza without a legend designating the material Highly Confidential shall not be subject to this Protective Order unless otherwise agreed by the parties and Alza or ordered by the Court, or otherwise designated Highly Confidential in accordance with the provisions of paragraph 10 of this Protective Order.

Access to Confidential Information

4. Documents and materials marked by Alza as "Highly Confidential" information may be disclosed only to the following Qualified Persons:

a. attorneys from the following firms who are currently of record in the present litigation:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.;
Morris, Nichols, Arsht & Tunnell;
Heller Ehrman LLP; and
Morris James LLP;

The addition or substitution of any attorneys as Qualified Persons beyond those identified in this paragraph may be made only upon written agreement of Alza. In no event shall any attorney involved in *Alza Corp. v Wyeth & Wyeth Pharmaceuticals, Inc.*, C.A. No. 9:06-CV-156-RHC, pending in the United States District Court for the Eastern District of Texas, Lufkin Division (or any related proceeding) (hereinafter "The Texas Litigation"), or in Reexamination Control Number 90/008,142, pending in the United States Patent and Trademark Office (or any related proceeding) (hereinafter "The Reexamination") have access to documents and material marked "Highly Confidential" by Alza.

b. independent litigation support service personnel, litigation consultants, outside exhibit preparation companies, or litigation study groups retained by a party for litigation

support with whom such outside counsel work in connection with this Proceeding to the extent such persons have a written agreement with outside counsel to maintain the confidentiality of their work, and provided that such personnel are regularly engaged in the provision of such services, and are not engaged in the research, development, manufacture, marketing, or sale of pharmaceutical products, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

c. any independent outside consultant or expert to the parties that is assisting outside counsel, is not a current employee of any of the parties in the litigation, and has been otherwise approved to see Confidential information in this litigation, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

d. the Court and any members of its staff to whom it is necessary to disclose Highly Confidential information for the purpose of assisting the Court in this Proceeding and stenographic employees, court reporters and typists for the sole purpose of recording, or transcribing testimony, documents or information relating to this Proceeding;

e. interpreters and translators for the sole purpose of recording, transcribing or translating testimony or documents relating to this Proceeding to the extent such persons have a written agreement with outside counsel to maintain the confidentiality of their work, and provided that such personnel are regularly engaged in the provision of such services, and are not engaged in the research, development, manufacture, marketing, or sale of pharmaceutical products, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

f. any person who prepared a particular document or thing, or who is listed on the document as a sender or recipient of the document, but the disclosure shall be limited to the specific Highly Confidential information disclosed in the particular document or thing.

As a condition precedent to disclosure of Highly Confidential information to independent outside consultants or experts referred to in subparagraph (c) above, counsel who retained the expert or consultant shall forward a copy of a written agreement to be bound by the terms of this Order and a copy of the expert's complete most recent curriculum vitae, including a list of publications, to counsel for Alza at least ten (10) court days prior to disclosure to such person. If Alza objects to the proposed disclosure within ten (10) court days after receipt of the notice, the disclosure may not be made without prior approval by the Court. Any objection shall state with particularity the basis for the objection.

5. Nothing contained in this Order shall preclude any party or Alza from using its own confidential information in any manner it sees fit, without prior consent of any party or the Court.

Inadvertent Production/Use of Confidential Information and Changes in Designation

6. Inadvertent production by Alza of any document or information without a designation of Highly Confidential will not be deemed to waive a later claim as to its confidential nature or stop Alza from designating said document or information as Highly Confidential.

7. Alza may change a designation to Highly Confidential (or withdraw a designation) regarding any material that it has produced. Such change in designation (or withdrawal) shall be accomplished by notifying counsel for each party in writing of such change in designation (or withdrawal). Upon receipt of any such written change in designation counsel of record shall: (i) not make any further disclosure or communication of such newly designated material except as provided for in this Order; (ii) take reasonable steps to notify any persons known to have

possession of any material with the original designation of the effect of such a change in designation under this Order; and (iii) promptly retrieve all copies and transcriptions of such originally designated material from any persons known to have possession of any such originally designated material who are not Qualified Persons under paragraph 3 above in light of the change of designation to the extent practicable. Properly marked documents shall be promptly provided by Alza of any such newly designated material.

8. If Highly Confidential information is disclosed to any person other than in the manner authorized by this Order, the party responsible for the disclosure shall within five (5) court days of learning of such disclosure inform Alza of all pertinent facts relating to such disclosure and shall obtain the prompt return of any such Highly Confidential information.

Inadvertent Production/Use of Privileged Information

9. If information subject to a claim of attorney-client privilege, attorney work product immunity or other legal privilege protecting information from discovery is inadvertently produced by Alza in any way, such production shall not prejudice or otherwise constitute a waiver (subject matter or otherwise) of, or estoppel as to, any claim of privilege, work product immunity, or other ground for withholding production to which the producing party or other person otherwise would be entitled. If a written claim of inadvertent production is made by a Alza pursuant to this paragraph the parties shall:

(a) not make any further copies or other reproductions or transcriptions of the inadvertently disclosed information or document; and

(b) destroy or return to Alza every original and every copy, reproduction, or transcription of all such inadvertently produced information or documents.

Alza's Disclosure of Information of Third-Parties Pursuant to the Subpoena

10. Any documents Alza produces in response to the Subpoena that are subject to confidentiality agreements between Alza and Plaintiff Wyeth shall be designated as Highly Confidential and may be produced pursuant to this Order without objection by Wyeth.

11. Any party that is served with a subpoena or other notice compelling the production of any Highly Confidential materials produced by Alza is obligated to give prompt telephonic and written notice (by hand delivery, courier or facsimile transmission) to Alza of such subpoena or other notice. In any event, such notice shall be given within five (5) court days of service of the subpoena or other notice. If Alza takes steps to oppose the subpoena, then the party served with the subpoena shall not disclose the pertinent information until the Court has resolved the issue. Absent Court order, production or disclosure shall not be made before notice is given to the Alza and Alza has had at least ten (10) court days to react after receiving such notice. Upon receiving such notice, Alza shall bear the burden to oppose, if it deems appropriate, the subpoena on grounds of confidentiality.

Use of Highly Confidential Information in Filings and in Open Court

12. Nothing herein shall be construed to affect in any manner the admissibility at trial or any other proceeding of any document, testimony, or other evidence.

13. The Clerk of the Court is directed to maintain under seal any pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a discovery request, or other paper filed with the Court that has been designated, in whole or in part, as containing or revealing Highly Confidential information.

14. In the event that a party wishes to use any Highly Confidential information in any pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a

discovery request, or other paper filed with the Court, such paper shall be enclosed in a sealed envelope or other appropriate container. The sealed envelope or other appropriate container shall:

(a) show the caption of this action;

(b) identify its contents; and

(c) include the following legend:

> HIGHLY CONFIDENTIAL INFORMATION PURSUANT TO STIPULATED PROTECTIVE ORDER: This envelope [or container] is sealed pursuant to court order and contains confidential information. The contents of this envelope must not be shown to any person except as authorized by the Protective Order Regarding the Production of Documents by Alza Corporation in Response to Subpoena in this action.

15. To the extent that a party (or a witness called by a party) contemplates using Highly Confidential information, which was produced by Alza, at trial or a hearing in open court and to the extent that a party moves for or agrees to the unsealing of any previously sealed pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a discovery request, or other paper filed with the Court, the party shall have the obligation to provide notice in writing to Alza of its intent. Alza shall have at least ten (10) court days after receiving such notice to respond to that notice before any of its Highly Confidential may be unsealed or used by any party at trial or a hearing in open court. In the event that Alza objects to the use or unsealing of the information, the party wanting to use or unseal the information shall bear the burden of establishing the need for such use and the adequacy of the protection of such information. In lieu of moving to use the Highly Confidential information in open court, the party wishing to use the information may request (with prior notice to Alza) that the Court close those portions of the proceedings in which the Highly Confidential information is to be used to all persons except Court personnel and persons authorized to receive Highly Confidential information produced by Alza under this Order.

Disposition of Confidential Materials upon Conclusion of Proceeding

16. Upon the conclusion of this Proceeding, including any appeals related thereto, at the option of Alza, all information and documents designated by Alza as Highly Confidential and any and all copies and transcriptions thereof, shall either be destroyed or returned within ninety (90) calendar days to counsel for Alza, provided, however, that outside counsel may retain all documents and things that contain or reflect their attorney work product – e.g., notes, memoranda, drafts of pleadings, deposition summaries, document review summaries, documents reviewed in preparation for depositions, hearings, or trial whether introduced or not – all correspondence, all pleadings, all deposition transcripts, all expert reports, all deposition, hearing and trial exhibits, and all court-filed documents even though they contain Highly Confidential information, but such retained work product and documents shall remain subject to the terms of this Order. Accordingly, upon final termination of this action, no one other than outside counsel shall retain any information designated Highly Confidential by Alza. Any person or entity having received recordings, notes, memoranda, summaries or other written materials, and all copies thereof, relating to or containing Alza Highly Confidential information shall deliver to Alza a declaration confirming that all such Highly Confidential information and any copies thereof, any and all records, notes, memoranda, summaries or other written material regarding the Highly Confidential information (except for attorney work product and documents permitted to be retained by outside counsel as stated above), have either been destroyed or delivered to counsel for Alza in accordance with the terms of this Order.

Miscellaneous Provisions

17. This Order shall be binding upon the parties to this Proceeding and Alza, including their successor(s) and assigns, and their respective attorneys, agents, representatives, officers and employees.

18. This Order shall apply to all information and material produced by Alza in response to the Subpoena, including all information and material produced prior to the execution of this Order by the Court.

19. The parties and Alza acknowledge and agree that if any party hereto breaches, or threatens to commit a breach of any of the provisions of this Order, Alza shall have the right to seek appropriate remedies from the Court, which remedies shall be in addition to and not in lieu of, any other remedies available to Alza under law or in equity, to have the Order specifically enforced (without posting any bond), including, without limitation, the right to an entry against the breaching party of restraining orders and injunctions (preliminary and permanent) against breaches, threatened or actual, it being agreed and acknowledged that, in the event of any such breach or threatened breach, the breaching party is not entitled to a presumption that money damages or legal remedies are sufficient or adequate to remedy such a breach.

20. By written agreement of the parties and Alza, or upon motion (with notice to Alza) and order of the Court, the terms of this Order may be amended or modified except as provided in paragraph 4 hereof.

21. This Order shall survive termination of this Proceeding, including any final judgment, appeal, or settlement to the extent the Highly Confidential information is not or does not become known to the public.

22. Nothing in this Order shall prejudice the right of Alza to oppose production of any information for lack of relevance, privilege, or any ground other than confidentiality.

23. In the event that a new party is added, substituted, or otherwise brought into this Proceeding, this protective order will be binding on and inure to the benefit of the new party, subject to the right of the new party to seek relief from or modification of this protective order.

24. The entry of this Order does not prevent any party from seeking a further order of this Court pursuant to Federal Rule of Civil Procedure 26(c).

Dated: _____

The Honorable Joseph J. Farnan, Jr.
UNITED STATES DISTRICT JUDGE

Jack B. Blumenfeld (I.D. No. 1014)
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EXHIBIT 9

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF TEXAS
LUFKIN DIVISION

ALZA CORPORATION, a Delaware corporation PLAINTIFF, v. WYETH, a Delaware corporation, and WYETH PHARMACEUTICALS, INC., a Delaware corporation, DEFENDANTS.	C.A. No. 9:06cv156

DEFENDANTS' REPLY IN SUPPORT OF MOTION TO STAY PROCEEDINGS PENDING *EX PARTE* REEXAMINATION OF U.S. PATENT NO. 6,440,457 B1

Congress authorized reexamination to "permit *efficient resolution* of questions about the validity of issued patents *without recourse to expensive and lengthy litigation.*" (*See* Wyeth Mem. at 4 (emphasis added).) Nonetheless, Alza argues that expensive discovery and a trial of multiple issues (that need never occur) is preferable to a reexamination proceeding on a single, potentially dispositive, issue. Alza's argument proceeds from several flawed premises. It contends that this Court "routinely" denies motions to stay, but two recent decisions of this Court have granted a stay where the litigations had progressed far beyond the stage in this case. Alza also argues that litigation will provide a more efficient and comprehensive resolution of the dispute, but it ignores the fact that cancellation of Alza's patent in reexamination would terminate this action ***in its entirety*** without the need of discovery or further proceedings in this Court.[1] Finally, Alza has not demonstrated that it will be prejudiced by a stay.

[1] Upon the dismissal of Alza's claims following cancellation of the '457 patent in the reexamination, Wyeth would dismiss its counterclaims.

I. This Court's Precedents Support The Granting Of A Stay.

Alza argues that this Court routinely denies stays. The decisions it cites, however, do not support that proposition. In *DataTreasury v. First Data*, No. 5:03-CV-00039-DF (E.D. Tex. Apr. 26, 2006), the litigation had already been pending for three years, the claims had been construed, and the close of discovery was just months away. *Id.* at 2, 5. In the remaining *DataTreasury* decisions, stays were "denied without prejudice subject to refiling" because the cases were undergoing consolidation. *DataTreasury Corp. v. Small Value Payments Co.*, No. 2:04-CV-00085-DF at 2 (E.D. Tex. Aug. 18, 2006); *DataTreasury Corp. v. Viewpoint Archive Services, LLC*, No. 2:05-CV-00290-DF (E.D. Tex. Feb. 9. 2005). In *Broadcom*, the parties had previously fully litigated the validity and enforceability of the patent. Then, just 2½ months from the close of discovery, over 2½ years after the original suit started, and just "five days after the Court refused Broadcom's attempts to delay the trial," Broadcom requested a stay pending reexamination. *Broadcom Corp. v. Microtune, LP*, No. 4:03-CV-00159-PBN 3, 5 (E.D. Tex. Dec. 15, 2003). The instant case presents circumstances that contrast sharply with those cases and are closely analogous to recent cases in which stays have been granted. *See Antor v. Nokia*, No. 2:05-CV-00186-DF at 9 (E.D. Tex. Sept. 27, 2006)(granting stay when: (1) it was requested without delay, (2) "discovery was far from being complete", and (3) the trial date was not near); *Echostar Tech. Corp. v. Tivo, Inc.*, No. 5:05-CV-81-DF (E.D. Tex. July 14, 2006).

II. Awaiting A Decision From The Reexamination Is The Most Efficient Means Of Resolving This Dispute.

This case will provide the benefits that Congress envisioned when it created reexamination. As Alza makes clear in its Opposition, this litigation will require discovery and trial of multiple validity issues, as well as infringement, enforceability, willfulness, and damages issues. In contrast, the reexamination proceeding involves a single validity issue, which has

already been resolved adverse to Alza by the PTO Board of Appeals.[2] If the PTO maintains its position, Alza's Complaint (and, as noted above, Wyeth's counterclaims) would be dismissed without the need for any discovery or trial. This action would accordingly be resolved in its entirety by cancellation of Alza's patent following reexamination. Alza's Opposition also appears to be based on the false premise that the reexamination will not go forward if Wyeth's motion is denied. Because the reexamination will proceed in any event, denial of a stay would not increase efficiency but would instead result in two parallel proceedings where only one might be necessary.[3]

A stay of the case is also the only procedural mechanism for avoiding the possibility of a conflict between a judgment in this action and a decision by the PTO. The reexamination will continue even if Alza were to prevail in this action. *Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1428-29 (Fed. Cir. 1988). A subsequent cancellation of the patent in reexamination would, in Wyeth's view, void a judgment in Alza's favor under FED. R. CIV. P. 60, but this issue has not been squarely addressed by a Federal Circuit precedential opinion.[4] Presumably Alza would contend that a subsequent cancellation of its patent would not affect an earlier money judgment in its favor. Absent an unequivocal statement by Alza disavowing any such contention, Wyeth should

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[2] Alza wrongly argues that the PTO rejected Wyeth's argument that the rejection of substantially similar claims in related applications provides evidence that a substantial new question of patentability existed. Alza Mem. at 3, 14. The PTO simply stated that the correspondence with the PTO which contained the rejections did not itself constitute prior art (although the patents described in that correspondence did).

[3] In addition to preserving the resources of the Court, a stay would potentially save the parties more than $10 million. According to the AIPLA's report on litigation expenses, the *mean* cost of patent litigation in Texas in cases in which alleged damages exceeded $25 million dollars was almost $5 million per party. AIPLA Report of The Economic Survey 2005 at p. I-110. As compared to expensive litigation, the *ex parte* reexamination proceeding will be relatively inexpensive.

[4] *See Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 996 F.2d 1236 (Fed. Cir. 1993) (per curiam) (non-precedential), available at 1993 WL 172432 at *1 (reversing the district court's denial of a stay of a permanent injunction and stay of damages proceedings pending court proceedings in response to reexamination). The *Standard Havens* opinion addresses, but not does not resolve, what happens if a patent is cancelled after a damages award: "[I]f a final decision of unpatentability means the patent was void *ab initio*, then damages would also be precluded."

not be put at risk of being in the untenable situation of having to pay damages for alleged infringement of a cancelled patent.

Rather than supporting Alza's argument, the reexamination statistics Alza cites demonstrate that a stay would likely achieve the efficiencies envisioned by Congress. Those statistics show that, in 59% of reexaminations requested by third parties, the patentee had to amend at least some of the claims (Alza's patent only has one claim) and in 12% of reexaminations, all claims were canceled. (Alza Mem., Ex. 1 at 2.) Thus, 71% of these proceedings result in decisions adverse to the patentee. More importantly, the likelihood of cancellation of the sole claim of the '457 patent is even greater because claims substantially similar to that claim have been rejected by the PTO in related applications over the same prior art forming the basis for the reexamination order for the '457 patent.

In an effort to diffuse the clear efficiencies of reexamination, Alza conjures up examples of "hopelessly long" reexamination proceedings. Its "Chart of Federal Circuit Reexamination Appeals" does not, however, accurately portray the speed at which a reexamination will proceed today. (Alza Mem., Ex. 8.) All but one of the reexaminations Alza cites began in 1996 or earlier. In July 2005, the PTO instituted a new reexamination process designed to "improve timeliness and quality." http://www.uspto.gov/web/offices/com/speeches/05-38.htm. This case demonstrates the effectiveness of that procedure: The PTO ordered reexamination within 30 days of the September 6, 2006 filing date it accorded the request rather than waiting the full three-month period permitted by statute. 35 U.S.C. § 303(a).

III. Alza Will Suffer No Legal Prejudice From A Stay.

Alza does not dispute that money damages would constitute an adequate remedy for any injury it may suffer if Wyeth infringes the '457 patent. Alza's half-hearted argument that it requires discovery from Wyeth to determine if Alza has suffered irreparable harm (Alza Mem. at

6 n.3) borders on the frivolous. In light of the public interest in maintaining patient access to EFFEXOR XR®, the irreparable harm that Wyeth would suffer from an injunction, and the lack of harm to Alza (which does not practice the '457 patent), it is inconceivable that an injunction could enter under the standards set forth in *eBay v. MercExchange LLC*, __ U.S. __, 126 S. Ct. 1837 (2006).

Unable to point to any real harm, Alza argues that delay itself is prejudicial, and that it will be prejudiced by waiting for the PTO to rule. But that type of delay–waiting for a federal agency to determine a crucial factual matter on which the entire litigation depends–does not generate the type of prejudice that is regarded as relevant to a stay motion.[5] Delay by itself is not a cognizable form of "prejudice." *Photoflex Prods. v. Circa 3 LLC*, 2006 WL 1440363 at *2 (N.D. Cal. May 24, 2006). Indeed, if it were, then no stay would ever issue.

Finally, Alza's claim that it will be prejudiced by a lack of discovery from Wyeth cannot survive scrutiny. First, reexamination was designed to decide patentability in an *ex parte* proceeding without the need to resort to expensive discovery. Every day, in both reexamination and original prosecutions, the PTO decides issues of patentability without discovery or input from third parties. Alza can hardly complain of prejudice because the system operates in the way Congress intended.[6] Second, Alza's own conduct demonstrates that it will not be prejudiced by lack of discovery. When the PTO rejected Alza's substantially similar claims in the related applications, Alza did not argue that Wyeth's patent, development efforts, or commercial success

[5] Alza wrongly attempts to argue that it is prejudiced because Wyeth did not seek a reexamination earlier. The Board decision forming the centerpiece of Wyeth's reexamination request did not issue until October 26, 2005, at which time there was a Standstill Agreement in place between the parties which had been entered into in an attempt to settle this dispute. During the period of the Standstill Agreement, Wyeth had hoped that negotiation would lead to an amicable resolution to this dispute and had no reason to file the Request for Reexamination. Wyeth submitted its Request for Reexamination shortly after Alza terminated that agreement and filed this lawsuit.

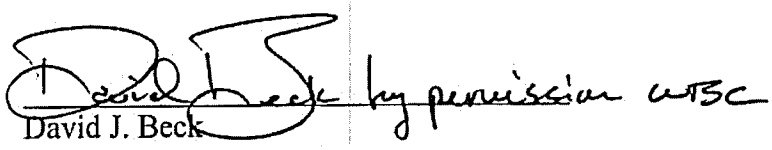
[6] Contrary to Alza's assertion, *Imax v. In-Three*, 385 F. Supp. 2d 1030, 1033 (C.D. Cal. 2005), while denying a stay, did not do so because of the need for discovery that could be used in a reexamination proceeding.

had any relevance to the patentability of the rejected claims, even though a substantial amount of this information was available to Alza.

For the foregoing reasons, Wyeth's Motion for Stay should be granted.

Dated: October 16, 2006

Respectfully submitted,



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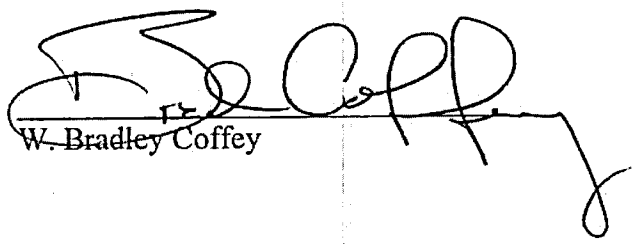
CERTIFICATE OF SERVICE

I hereby certify that a copy of the above and foregoing has been served upon all counsel of record in compliance with Rule 5b of the Federal Rules of civil Procedure this 16th day of October, 2006.



W. Bradley Coffey

EXHIBIT 10

Smedley, Tamara L.

From: Ernst, Samuel F.
Sent: Friday, February 23, 2007 1:59 PM
To: 'Jack B. Blumenfeld (jblumenfeld@mnat.com)'; 'klouden@mnat.com'; 'Basil J. Lewris (bill.lewris@finnegan.com)'; 'Rudolph, Barbara'
Cc: Thayer, M. Patricia; Wolff, Jessica R.; Kassabian, Daniel N.
Subject: Wyeth v. Impax: Alza subpoena

Contacts: Jack B. Blumenfeld
Attachments: Stipulated Protective Order.pdf

Counsel,
Counsel for Alza have agreed to the attached form of protective order to govern the production of documents in response to Impax's subpoena to Alza. Please advise us if Wyeth will agree to sign this protective order so that we may request the Court to enter it as a stipulation.

Stipulated Protective Order.pd..

Sam Ernst | Attorney | HellerEhrmanLLP | 333 Bush Street | San Francisco, CA 94104
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EXHIBIT 11

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March 5, 2007

Samuel F. Ernst, Esq.
Heller Ehrman LLP
333 Bush Street
San Francisco, CA 94140-2878

Via Facsimile

Wyeth v. Impax Laboratories, Inc., Civil Action No.: 06-222 (D. Del.)

Dear Samuel:

I am writing in response to your letter of February 23, 2007 enclosing a draft protective order regarding the production of documents by Alza in response to Impax's subpoena. We spent a significant amount of time negotiating a protective order with the ability to incorporate third parties. Why is this separate protective order which raises new issues being proposed? We await your response.

Sincerely,

Linda A. Wadler

LAW/amn

cc: Mary B. Matterer, Esq. (via Facsimile)

EXHIBIT 12

HellerEhrman LLP

March 6, 2007

Via Facsimile and electronic mail

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40443.0005

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Finnegan Henderson Farabow Garrett
& Dunner LLP
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Re: *Wyeth v. Impax Laboratories, Inc.*, No. 06-222 (D. Del.)

Dear Linda:

This is in response to your letter dated March 5, 2007 regarding the production of documents by Alza in response to our subpoena.

Alza reviewed the protective order that Impax and Wyeth had been negotiating for some months and that was recently entered by the Court, but Alza was dissatisfied with that form of order to govern the production of Alza documents in response to our subpoena. The protective order that we negotiated with Alza provides some additional protections for Alza confidential information (in particular, with regard to paragraph 4) to ensure that documents Alza produces in this litigation are not used for the purpose of any other litigation or proceeding. We feel this is entirely appropriate. Under Federal Rule of Civil Procedure 45(c)(3)(B), Alza has the right to pursue additional or different forms of protection for confidential information produced in response to a subpoena than those protections to which the parties to the litigation have agreed.

Please review the form of order (enclosed again for your convenience) and let us know this week whether Wyeth agrees to the form of order. If Wyeth does not agree, then we will move the Court for entry of the order.

On a separate matter, nobody at our firm received your fax of March 5 to which this letter responds. Because this problem has occurred repeatedly, you should not assume that we have received faxes you send. In the future, we suggest that both parties send correspondence as PDF files attached to e-mails.

Best regards,

Samuel F. Ernst

Enclosure

cc: Basil J. Lewris, Esq.
Barbara R. Rudolph, PhD.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

WYETH, Plaintiff, v. IMPAX LABORATORIES, INC., Defendant.	Civil Action No.: 06-222 (JJF)

STIPULATED PROTECTIVE ORDER REGARDING THE PRODUCTION OF DOCUMENTS BY ALZA CORPORATION IN RESPONSE TO SUBPOENA

WHEREAS, Defendant Impax Pharmaceuticals served on third party Alza Corporation ("Alza") a subpoena issued by the District Court for the Northern District of California, ("the Subpoena"), requesting the production of certain documents and information for use in the above-styled proceeding (the "Proceeding"), many of which contain trade secrets, or other confidential and proprietary, scientific, technical, financial, strategic, business planning, business arrangement, competitive, research, development, or other kinds of commercially sensitive information within the meaning of Federal Rule of Civil Procedure 26(c)(7);

WHEREAS, Alza and the parties, through their respective counsel, have agreed that a Stipulated Protective Order preserving the confidentiality of certain documents and information produced in response to the Subpoena should be entered by the United States District Court for the District of Delaware; and

WHEREAS, the parties have established good cause for entry of this Stipulated Protective Order;

IT IS HEREBY STIPULATED AND AGREED, SUBJECT TO THE APPROVAL AND ORDER OF THE COURT THAT:

1. Alza may designate as "Highly Confidential" all or any part of any discovery and other materials produced in response to the Subpoena that contain sensitive financial, patent, trademark, copyright, trade secret, marketing, customer, research, manufacture, regulatory, commercial, business, strategic, or product development information, or any other confidential technical or non-technical information or know-how of such a nature as to be protectable under Federal Rule of Civil Procedure 26(c)(7).

2. Material designated by Alza as Highly Confidential information, including all information derived therefrom, and all copies, summaries, abstracts, excerpts, indices, and descriptions of such material shall be held in confidence by the receiving party, shall be used only by persons permitted access to it under this Protective Order, and shall not be used for any purpose other than in connection with this litigation or appeal of this proceeding. Material designated by Alza as Highly Confidential information shall not be used for any research, development, manufacture, patent filing or prosecution, financial purpose, commercial purpose, marketing purpose, business purpose, regulatory purpose, Citizen's Petitions, lawsuits against the FDA, or any other litigation, regulatory or administrative proceeding, mediation or arbitration.

Designation Procedure

3. Designation by Alza of a document or thing as Highly Confidential information shall be made by stamping it with the legend "HIGHLY CONFIDENTIAL" or "HIGHLY CONFIDENTIAL SUBJECT TO PROTECTIVE ORDER" as reasonably appropriate when it is produced. Anything that cannot be so marked on its face shall be marked by placing the appropriate legend on a container or package in which the thing is produced or on a tag attached

thereto. Each page of each document and each thing produced in response to the Subpoena shall bear an identifying number.

Documents and things produced by Alza without a legend designating the material Highly Confidential shall not be subject to this Protective Order unless otherwise agreed by the parties and Alza or ordered by the Court, or otherwise designated Highly Confidential in accordance with the provisions of paragraph 10 of this Protective Order.

Access to Confidential Information

4. Documents and materials marked by Alza as "Highly Confidential" information may be disclosed only to the following Qualified Persons:

a. attorneys from the following firms who are currently of record in the present litigation:

Finnegan, Henderson, Farabow, Garrett & Dunner, L.L.P.;
Morris, Nichols, Arsht & Tunnell;
Heller Ehrman LLP; and
Morris James LLP;

The addition or substitution of any attorneys as Qualified Persons beyond those identified in this paragraph may be made only upon written agreement of Alza. In no event shall any attorney involved in *Alza Corp. v Wyeth & Wyeth Pharmaceuticals, Inc.*, C.A. No. 9:06-CV-156-RHC, pending in the United States District Court for the Eastern District of Texas, Lufkin Division (or any related proceeding) (hereinafter "The Texas Litigation"), or in Reexamination Control Number 90/008,142, pending in the United States Patent and Trademark Office (or any related proceeding) (hereinafter "The Reexamination") have access to documents and material marked "Highly Confidential" by Alza.

b. independent litigation support service personnel, litigation consultants, outside exhibit preparation companies, or litigation study groups retained by a party for litigation

support with whom such outside counsel work in connection with this Proceeding to the extent such persons have a written agreement with outside counsel to maintain the confidentiality of their work, and provided that such personnel are regularly engaged in the provision of such services, and are not engaged in the research, development, manufacture, marketing, or sale of pharmaceutical products, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

c. any independent outside consultant or expert to the parties that is assisting outside counsel, is not a current employee of any of the parties in the litigation, and has been otherwise approved to see Confidential information in this litigation, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

d. the Court and any members of its staff to whom it is necessary to disclose Highly Confidential information for the purpose of assisting the Court in this Proceeding and stenographic employees, court reporters and typists for the sole purpose of recording, or transcribing testimony, documents or information relating to this Proceeding;

e. interpreters and translators for the sole purpose of recording, transcribing or translating testimony or documents relating to this Proceeding to the extent such persons have a written agreement with outside counsel to maintain the confidentiality of their work, and provided that such personnel are regularly engaged in the provision of such services, and are not engaged in the research, development, manufacture, marketing, or sale of pharmaceutical products, provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination;

f. any person who prepared a particular document or thing, or who is listed on the document as a sender or recipient of the document, but the disclosure shall be limited to the specific Highly Confidential information disclosed in the particular document or thing.

As a condition precedent to disclosure of Highly Confidential information to independent outside consultants or experts referred to in subparagraph (c) above, counsel who retained the expert or consultant shall forward a copy of a written agreement to be bound by the terms of this Order and a copy of the expert's complete most recent curriculum vitae, including a list of publications, to counsel for Alza at least ten (10) court days prior to disclosure to such person. If Alza objects to the proposed disclosure within ten (10) court days after receipt of the notice, the disclosure may not be made without prior approval by the Court. Any objection shall state with particularity the basis for the objection.

5. Nothing contained in this Order shall preclude any party or Alza from using its own confidential information in any manner it sees fit, without prior consent of any party or the Court.

Inadvertent Production/Use of Confidential Information and Changes in Designation

6. Inadvertent production by Alza of any document or information without a designation of Highly Confidential will not be deemed to waive a later claim as to its confidential nature or stop Alza from designating said document or information as Highly Confidential.

7. Alza may change a designation to Highly Confidential (or withdraw a designation) regarding any material that it has produced. Such change in designation (or withdrawal) shall be accomplished by notifying counsel for each party in writing of such change in designation (or withdrawal). Upon receipt of any such written change in designation counsel of record shall: (i) not make any further disclosure or communication of such newly designated material except as provided for in this Order; (ii) take reasonable steps to notify any persons known to have

possession of any material with the original designation of the effect of such a change in designation under this Order; and (iii) promptly retrieve all copies and transcriptions of such originally designated material from any persons known to have possession of any such originally designated material who are not Qualified Persons under paragraph 3 above in light of the change of designation to the extent practicable. Properly marked documents shall be promptly provided by Alza of any such newly designated material.

8. If Highly Confidential information is disclosed to any person other than in the manner authorized by this Order, the party responsible for the disclosure shall within five (5) court days of learning of such disclosure inform Alza of all pertinent facts relating to such disclosure and shall obtain the prompt return of any such Highly Confidential information.

Inadvertent Production/Use of Privileged Information

9. If information subject to a claim of attorney-client privilege, attorney work product immunity or other legal privilege protecting information from discovery is inadvertently produced by Alza in any way, such production shall not prejudice or otherwise constitute a waiver (subject matter or otherwise) of, or estoppel as to, any claim of privilege, work product immunity, or other ground for withholding production to which the producing party or other person otherwise would be entitled. If a written claim of inadvertent production is made by a Alza pursuant to this paragraph the parties shall:

(a) not make any further copies or other reproductions or transcriptions of the inadvertently disclosed information or document; and

(b) destroy or return to Alza every original and every copy, reproduction, or transcription of all such inadvertently produced information or documents.

Alza's Disclosure of Information of Third-Parties Pursuant to the Subpoena

10. Any documents Alza produces in response to the Subpoena that are subject to confidentiality agreements between Alza and Plaintiff Wyeth shall be designated as Highly Confidential and may be produced pursuant to this Order without objection by Wyeth.

11. Any party that is served with a subpoena or other notice compelling the production of any Highly Confidential materials produced by Alza is obligated to give prompt telephonic and written notice (by hand delivery, courier or facsimile transmission) to Alza of such subpoena or other notice. In any event, such notice shall be given within five (5) court days of service of the subpoena or other notice. If Alza takes steps to oppose the subpoena, then the party served with the subpoena shall not disclose the pertinent information until the Court has resolved the issue. Absent Court order, production or disclosure shall not be made before notice is given to the Alza and Alza has had at least ten (10) court days to react after receiving such notice. Upon receiving such notice, Alza shall bear the burden to oppose, if it deems appropriate, the subpoena on grounds of confidentiality.

Use of Highly Confidential Information in Filings and in Open Court

12. Nothing herein shall be construed to affect in any manner the admissibility at trial or any other proceeding of any document, testimony, or other evidence.

13. The Clerk of the Court is directed to maintain under seal any pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a discovery request, or other paper filed with the Court that has been designated, in whole or in part, as containing or revealing Highly Confidential information.

14. In the event that a party wishes to use any Highly Confidential information in any pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a

discovery request, or other paper filed with the Court, such paper shall be enclosed in a sealed envelope or other appropriate container. The sealed envelope or other appropriate container shall:

(a) show the caption of this action;

(b) identify its contents; and

(c) include the following legend:

> HIGHLY CONFIDENTIAL INFORMATION PURSUANT TO STIPULATED PROTECTIVE ORDER: This envelope [or container] is sealed pursuant to court order and contains confidential information. The contents of this envelope must not be shown to any person except as authorized by the Protective Order Regarding the Production of Documents by Alza Corporation in Response to Subpoena in this action.

15. To the extent that a party (or a witness called by a party) contemplates using Highly Confidential information, which was produced by Alza, at trial or a hearing in open court and to the extent that a party moves for or agrees to the unsealing of any previously sealed pleading, motion, brief, memorandum, exhibit, affidavit, declaration, transcript, response to a discovery request, or other paper filed with the Court, the party shall have the obligation to provide notice in writing to Alza of its intent. Alza shall have at least ten (10) court days after receiving such notice to respond to that notice before any of its Highly Confidential may be unsealed or used by any party at trial or a hearing in open court. In the event that Alza objects to the use or unsealing of the information, the party wanting to use or unseal the information shall bear the burden of establishing the need for such use and the adequacy of the protection of such information. In lieu of moving to use the Highly Confidential information in open court, the party wishing to use the information may request (with prior notice to Alza) that the Court close those portions of the proceedings in which the Highly Confidential information is to be used to all persons except Court personnel and persons authorized to receive Highly Confidential information produced by Alza under this Order.

Disposition of Confidential Materials upon Conclusion of Proceeding

16. Upon the conclusion of this Proceeding, including any appeals related thereto, at the option of Alza, all information and documents designated by Alza as Highly Confidential and any and all copies and transcriptions thereof, shall either be destroyed or returned within ninety (90) calendar days to counsel for Alza, provided, however, that outside counsel may retain all documents and things that contain or reflect their attorney work product – e.g., notes, memoranda, drafts of pleadings, deposition summaries, document review summaries, documents reviewed in preparation for depositions, hearings, or trial whether introduced or not – all correspondence, all pleadings, all deposition transcripts, all expert reports, all deposition, hearing and trial exhibits, and all court-filed documents even though they contain Highly Confidential information, but such retained work product and documents shall remain subject to the terms of this Order. Accordingly, upon final termination of this action, no one other than outside counsel shall retain any information designated Highly Confidential by Alza. Any person or entity having received recordings, notes, memoranda, summaries or other written materials, and all copies thereof, relating to or containing Alza Highly Confidential information shall deliver to Alza a declaration confirming that all such Highly Confidential information and any copies thereof, any and all records, notes, memoranda, summaries or other written material regarding the Highly Confidential information (except for attorney work product and documents permitted to be retained by outside counsel as stated above), have either been destroyed or delivered to counsel for Alza in accordance with the terms of this Order.

Miscellaneous Provisions

17. This Order shall be binding upon the parties to this Proceeding and Alza, including their successor(s) and assigns, and their respective attorneys, agents, representatives, officers and employees.

18. This Order shall apply to all information and material produced by Alza in response to the Subpoena, including all information and material produced prior to the execution of this Order by the Court.

19. The parties and Alza acknowledge and agree that if any party hereto breaches, or threatens to commit a breach of any of the provisions of this Order, Alza shall have the right to seek appropriate remedies from the Court, which remedies shall be in addition to and not in lieu of, any other remedies available to Alza under law or in equity, to have the Order specifically enforced (without posting any bond), including, without limitation, the right to an entry against the breaching party of restraining orders and injunctions (preliminary and permanent) against breaches, threatened or actual, it being agreed and acknowledged that, in the event of any such breach or threatened breach, the breaching party is not entitled to a presumption that money damages or legal remedies are sufficient or adequate to remedy such a breach.

20. By written agreement of the parties and Alza, or upon motion (with notice to Alza) and order of the Court, the terms of this Order may be amended or modified except as provided in paragraph 4 hereof.

21. This Order shall survive termination of this Proceeding, including any final judgment, appeal, or settlement to the extent the Highly Confidential information is not or does not become known to the public.

22. Nothing in this Order shall prejudice the right of Alza to oppose production of any information for lack of relevance, privilege, or any ground other than confidentiality.

23. In the event that a new party is added, substituted, or otherwise brought into this Proceeding, this protective order will be binding on and inure to the benefit of the new party, subject to the right of the new party to seek relief from or modification of this protective order.

24. The entry of this Order does not prevent any party from seeking a further order of this Court pursuant to Federal Rule of Civil Procedure 26(c).

Dated: _____

The Honorable Joseph J. Farnan, Jr.
UNITED STATES DISTRICT JUDGE

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EXHIBIT 13

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March 7, 2007

Via Facsimile

Steven R. Trybus, Esq.
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330 N. Wabash Avenue
Chicago, IL 60611

Wyeth v. Impax Laboratories, Inc., Civil Action No.: 06-222 (D. Del.)

Dear Steven:

I am writing in response to a draft protective order sent to us by Impax counsel regarding the production of documents by Alza in response to Impax's subpoena. Regrettably, we were not included in any discussions leading up to that draft. As written, the draft is not acceptable. We suggest the following changes for Alza's consideration:

delete the last sentence of paragraph 4(a);

delete the phrase ", provided that no person identified in this subparagraph shall have any involvement in The Texas Litigation or The Reexamination" in paragraphs 4(b), 4(c), and 4(e);

permitting two in-house counsel from Wyeth (Susan Lee and Lawrence Alaburda) access to documents produced by Alza under the provisions of the protective order;

Insert a new paragraph after paragraph 5 stating:

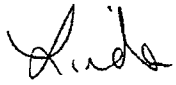
> "Nothing contained in this Order shall preclude disclosure to current or former Wyeth employees of Wyeth documents to which Wyeth has already had access, including but not limited to the following categories of documents produced by Alza:
>
> 1. correspondence between Wyeth and Alza;
>
> 2. documents where one or more Wyeth employees are listed on the document as an author, sender, or recipient of the document; and

3. documents which originated from Wyeth's files."

Insert the words "to Wyeth and Impax" after the word "produced" in the last line of Paragraph 10.

Please feel free to call me or Barbara Rudolph to discuss this matter if you believe it would be helpful in reaching a resolution more promptly. In the meantime, we await your response.

Sincerely,



Linda A. Wadler

LAW/sas

cc: Mary B. Matterer, Esq. (via e-mail)
Samuel F. Ernst, Esq. (Via e-mail)

EXHIBIT 14

HellerEhrman LLP

March 8, 2007

Via E-mail

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40443.0005

Linda A. Wadler, Esq.
Finnegan Henderson Farabow Garrett
& Dunner LLP
901 New York Ave., NW
Washington, DC 20001-4413

Re: *Wyeth v. Impax Laboratories, Inc.*, Civil Action No. 06-222 (D. Del.)

Dear Linda:

This is in regard to your letter of March 7, 2007 to Mr. Trybus regarding the protective order Impax and Alza have negotiated to govern the production of documents in response to the subpoena Impax served on Alza.

Alza's counsel reviewed the draft protective order entered in this action and found that it lacked adequate protections. Alza was particularly concerned that their documents should remain "outside counsel eyes only" and that Wyeth counsel in this litigation should not work on the Alza/Wyeth litigation because it is impossible for a person to compartmentalize his mind between cases. Please explain why Wyeth has any interest in broadening the disclosure of highly confidential Alza documents produced in response to this subpoena.

Counsel for Impax worked hard with counsel for Alza to negotiate an order governing the production of these documents. We feel the protections Alza has requested are appropriate and we can conceive of no legitimate interest Wyeth would have in diluting these protections.

Accordingly, if you do not stipulate to the Alza protective order by March 15, 2007, we will ask the Court to enter the order Impax and Alza have agreed to. In order to avoid the delay in receiving these documents pending the resolution of our motion, we ask that Wyeth

agree to a stipulation that it will be bound to the terms of the order Alza and Impax have negotiated pending the Court's resolution of Impax's motion. To avoid unnecessary delay in discovery, please let us know immediately if you agree to such a stipulation.

Sincerely,

Samuel F. Ernst

cc: Steven R. Trybus, Esq.

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EXHIBIT 15

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March 12, 2007

Via E-mail

Samuel F. Ernst, Esq.
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333 Bush Street
San Francisco, CA 94140-2878

Wyeth v. Impax Laboratories, Inc., Civil Action No.: 06-222 (D. Del.)

Dear Samuel:

I am writing in response to your letter of March 8, 2007. We have reached out by telephone to Mr. Trybus as a follow up to our letter of March 7th to him and are waiting for his response. Your setting of a March 15th deadline for Wyeth to conclude its negotiations with Alza is both arbitrary and inappropriate. Although "[c]ounsel for Impax [may have] worked hard with counsel for Alza to negotiate an order governing the production of these documents," Impax elected to negotiate a separate protective order with Alza without including us in those negotiations. As a result, any delay resulting from Wyeth's need to separately negotiate with Alza is the result of that Impax decision.

Sincerely,

Linda A. Wadler

LAW/sas

cc: Mary B. Matterer, Esq. (via e-mail)
Steven Trybus, Esq. (via e-mail)

EXHIBIT 16

HellerEhrman LLP

March 13, 2007

Via E-mail

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40443.0005

Linda A. Wadler, Esq.
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901 New York Ave., NW
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Re: *Wyeth v. Impax Laboratories, Inc.*, No. 06-222 (D. Del.)

Dear Linda:

This is in response to you letter of March 12, 2007.

Impax did not include Wyeth in the negotiations with Alza surrounding the protections to govern the Alza documents produced in response to our subpoena because we could conceive of no legitimate interest Wyeth could have in the protections surrounding these documents. These are not Wyeth's documents. These documents are not being produced in response to Wyeth's subpoena.

Please advise us as to whether you have reached an agreement with Alza regarding the form of this protective order by close of business Thursday. Our deadline is not arbitrary – we need to get our motion for entry of the order on file in order to be heard at the April 13 hearing for non-dispositive motions.

Best regards,

Samuel F. Ernst

cc: Steven Trybus, Esq.

EXHIBIT 17

IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
LUFKIN DIVISION

ALZA CORPORATION	§	
	§	
Plaintiff,	§	
	§	Civil Action No. 9:06-CV-156
v.	§	
	§	
WYETH and WYETH PHARMACEUTICALS, INC.	§	JUDGE RON CLARK
	§	
	§	
Defendant.	§	

ORDER GRANTING DEFENDANT'S MOTION TO STAY

Before the court is Defendant's Motion to Stay [Doc. #15] seeking to stay this case until the United States Patent and Trademark Office ("PTO") concludes its reexamination of the patent-in-suit.

I. Facts and Procedural History

Plaintiff Alza Corporation ("Alza") is the owner of United States Patent No. 6,440,457 B1 ("the '457 patent"). On July 26, 2006, Alza filed a suit against Defendants Wyeth and Wyeth Pharmaceuticals, Inc. (collectively, "Wyeth") alleging that Wyeth infringed Claim 1 of the '457 patent by selling Effexor® XR, a pharmaceutical product which Wyeth has sold since 1997.

On July 28, 2006, Wyeth filed a request for reexamination with the PTO of the '457 patent. On October 2, 2006, the PTO granted the request and ordered reexamination of the '457 patent. Reexamination is a procedure that allows the PTO to reconsider the validity of an existing patent. 35 U.S.C. §§ 301, *et seq.* Wyeth now moves to stay this litigation pending the outcome of the reexamination proceeding.

II. Analysis

Reexamination of patent validity in the PTO is a "useful and necessary alternative for challengers and for patent owners to test the validity of United States patents in an efficient and relatively inexpensive manner." H.Rep. No. 96-1307(I), at 4. As the Federal Circuit has explained, "[o]ne purpose of the reexamination procedure is to eliminate trial of that issue . . . or to facilitate trial of that issue." *Gould v. Control Laser Corp.*, 705 F.2d 1340, 1342 (Fed. Cir. 1983).

This court has the inherent power to control its own docket, including the power to stay proceedings. *Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1426 (Fed. Cir. 1988). In deciding whether to stay litigation pending reexamination, this court considers: 1) whether a stay would unduly prejudice or present a clear tactical disadvantage to the nonmoving party; 2) whether a stay will simplify the issues in question and trial of the case; and 3) whether discovery is complete and whether a trial date has been set. *EchoStar Technologies Corp. v. Tivo, Inc.*, 2006 WL 2501494 (E.D. 2006).

1. Prejudice or Disadvantage to Plaintiff

Plaintiff argues that "the PTO reexamination proceeding cannot resolve the entire dispute between the parties and will take years to resolve." In addition, Plaintiff contends that a stay is not warranted because certain evidence of the non-obviousness of the '457 patent is in Defendants' possession and discovery would be unavailable to Plaintiff in the reexamination proceeding.

Reexamination does not threaten protracted or indefinite delay. The reexamination statute directs the PTO to conduct reexamination proceedings with "special dispatch." 35 U.S.C. § 305. Additionally, because the patent is involved in litigation, the reexamination proceeding

will "have priority over all other cases." Manual of Patent Examining Procedures § 2261.

This case is still in its infancy. Discovery has not begun and the scheduling conference is set for December 8, 2006. The parties have not yet submitted a Rule 26(f) Joint Conference Report. Therefore, this is not a case in which the parties have already invested substantial time and resources in litigation. *Cf. Soverain Software LLC v. Amazon.com,* 356 F.Supp. 2d 660, 662 (E.D. Tex. 2005)(denying stay where the case was a year old and the court had already held a *Markman* hearing). Furthermore, if the parties continue to litigate the validity of claims in this court and the PTO subsequently finds that the claim in issue is invalid, this action would be moot and the parties will have wasted all of its time and resources. Thus, granting the stay will maximize the likelihood that assets need not be expended to address invalid claims.

Although Plaintiff claims that it will be prejudiced because the PTO does not allow discovery in its reexamination proceeding, this court will not second-guess a system designed by Congress that has operated without discovery for many years. Therefore, this factor weighs in favor of granting a stay.

2. Simplification of Case

Plaintiff contends that reexamination will not simplify issues for trial because the PTO will address only the obviousness of the '457 patent whereas this court is able to resolve this dispute in its entirety.

Plaintiff fails to consider the potential positive effects a PTO reexamination. Allowing issues of validity to be evaluated by the PTO makes sense because "the PTO may be in a better position than the Court to evaluate the validity of a patent in view of prior art references. *GPAC v. D.W.W. Enterprises, Inc.,* 144 F.R.D. 60, 63 (1992). Also, regardless of the reexamination result, allowing the PTO to reexamine first should simplify and streamline the issues in this

litigation. Put simply, "courts need not expend unnecessary judicial resources by attempting to resolve claims which may be amended, eliminated or lucidly narrowed by the patent reexamination process and the expertise of its officers." *Hewlett-Packard Co. v. Acuson Corp.*, 1993 WL 149994, at *2 (N.D. Cal. May 5, 1993). Statistically, 71% of reexamination proceedings result in amended or cancelled claims. Therefore, as a matter of judicial efficiency and economy, it makes sense to await the conclusion of a reexamination before resuming the instant litigation.

Furthermore, the issue of claim construction will be simplified if a stay is granted. Because statements made during the reexamination proceedings become part of the prosecution history, a stay will allow the intrinsic evidence to be fully developed before this court begins the claim construction process. *See E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1439 (Fed. Cir. 1988)(holding that statements made during reexamination proceeding are relevant prosecution history when interpreting claims.) Therefore, this factor weighs in favor of granting a stay.

3. Completion of Discovery and Trial Date

Plaintiff admits that this case is in the early stages of litigation. However, Plaintiff argues that because this court has set a trial date, the factor weighs heavily in its favor. Here, the scheduling conference has not been held and discovery proceedings have not commenced. No dispositive motions have been submitted and no significant issues have been resolved.

Perhaps most importantly, the claim construction process has not begun. None of the parties have proposed claim construction definitions or submitted claim construction briefs and a *Markman* hearing is not until October 26, 2007. Although a trial date has been proposed to the parties, it is March 10, 2008, about sixteen months from now. Therefore, this factor also weighs

in favor of granting a stay.

III. Conclusion

Based on the foregoing, this court finds that the benefits of granting Defendant's Motion to stay outweigh the burdens of delay caused by a reexamination proceeding in this case.

IT IS THEREFORE ORDERED that Defendant's Motion to Stay is **GRANTED.** The case shall be stayed pending a decision by the PTO or until further order of this court. The parties shall notify this court of any significant change in the status of the proceeding before the PTO, and of any decision by the PTO.

IT IS FURTHER ORDERED that the Case Management Conference scheduled for December 8, 2006 is **CANCELLED.**

So **ORDERED** and **SIGNED** this **21** day of **November, 2006.**

Ron Clark

Ron Clark, United States District Judge